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A RESEARCH ON REGULATORY PATHWAYS FOR BIOSIMILAR PRODUCT REGISTRATION FOR UNITED STATES, COLOMBIA, AND THE PHILIPPINES

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ABSTRACT

Biosimilars have emerged as an essential component of modern healthcare systems by improving patient access to high-cost biological therapies while maintaining standards of quality, safety, and efficacy. Due to the inherent complexity of biological products, biosimilars require distinct regulatory pathways that differ significantly from those applied to conventional small-molecule generics. Regulatory frameworks governing biosimilar products vary across countries, reflecting differences in legal structures, regulatory maturity, and public health priorities. This review provides a comprehensive and comparative analysis of biosimilar product registration pathways in the United States, Colombia, and the Philippines. These jurisdictions were selected to represent a highly regulated market, a Latin American regulatory system with defined biosimilar legislation, and a Southeast Asian regulatory system incorporating reliance and regional harmonization approaches. The review examines key regulatory elements including legal frameworks, regulatory authorities, biosimilar approval pathways, dossier structure and submission requirements, reference product acceptability, and post-approval obligations. Special emphasis is placed on the role of the Common Technical Document–based dossier architecture and the practical reuse of core quality documents such as specifications and

Certificates of Analysis across multiple jurisdictions. The analysis highlights both convergence and divergence in regulatory expectations, with all three systems adopting a comparability-based, stepwise evaluation approach while differing in procedural implementation and reliance mechanisms. The findings of this review aim to support regulatory professionals, researchers, and pharmaceutical manufacturers in developing efficient biosimilar registration strategies and in understanding evolving global trends in biosimilar regulation.

KEYWORDS: Biosimilars, Biologics, Regulatory pathways, Biosimilar registration, CTD dossier, United States, Colombia, Philippines.

INTRODUCTION

1. INTRODUCTION

Biological medicinal products have transformed the management of chronic, life-threatening, and immune-mediated diseases by offering highly targeted therapeutic options. Unlike conventional small-molecule drugs, biological products are derived from living systems and exhibit complex molecular structures, inherent variability, and sensitivity to manufacturing processes. These characteristics present unique challenges for product development, quality control, and regulatory oversight.[1,2]

1.1 Biologics: Definition and Regulatory Complexity

Biologics are medicinal products produced using biological sources such as living cells or organisms through biotechnological processes. They typically include proteins, monoclonal antibodies, hormones, vaccines, and other complex macromolecules. The clinical performance of biologics is closely linked to their manufacturing process, making complete molecular characterization and exact replication impractical. As a result, regulatory evaluation of biologics places significant emphasis on process control, quality consistency, and lifecycle management.[1,3]

1.2 Biosimilars: Concept and Distinction from Generics

Biosimilars are biological products that are highly similar to an already authorized reference biological product, with no clinically meaningful differences in terms of safety, quality, and efficacy. Unlike generic drugs, which are chemically identical to their reference products, biosimilars cannot be considered identical due to the intrinsic variability of biological systems. Consequently, biosimilar approval relies on a comparability-based regulatory

approach rather than demonstration of bioequivalence alone.[1,4] The development and evaluation of biosimilars involve a stepwise process that begins with extensive analytical characterization and is followed by targeted non-clinical and clinical studies, as necessary, to address residual uncertainty. This approach ensures that biosimilars meet the same standards of clinical performance as their reference products while avoiding unnecessary duplication of studies.[1,5]

1.3 Rationale and Scope of the Review

Despite increasing global experience with biosimilars, regulatory requirements and approval pathways continue to vary across jurisdictions. Understanding these differences is particularly important for pharmaceutical manufacturers pursuing multi-country registration strategies and for regulators aiming to strengthen biosimilar oversight.[6] This review focuses on a comparative evaluation of biosimilar product registration pathways in the United States, Colombia, and the Philippines. These countries represent diverse regulatory environments and provide valuable insights into how common scientific principles are implemented through different legal and procedural frameworks. The review aims to analyse regulatory pathways, dossier requirements, and practical considerations for biosimilar registration, while highlighting areas of convergence, divergence, and future harmonization.[6,7]

Steps Involved in Development and Evaluation of Biosimilars

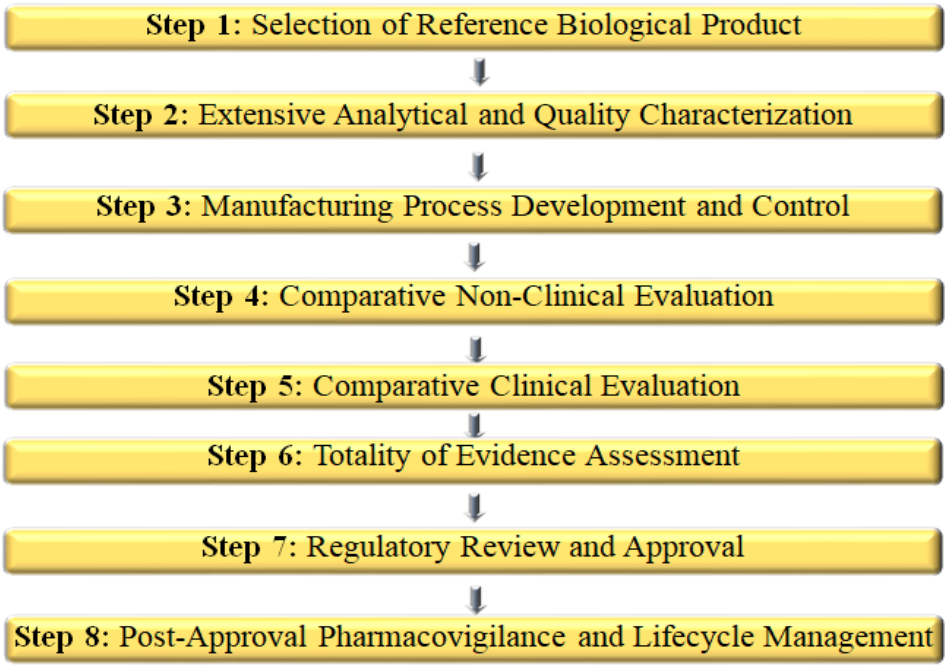

Figure 1.1: Stepwise Development and Evaluation of Biosimilars.

BIOSIMILAR PRODUCT REGISTRATION DOSSIER AND REGULATORY DOSSIER ARCHITECTURE

2. Biosimilar Product Registration Dossier: Structure and Regulatory Rationale

Regulatory evaluation of biosimilar products is based on a comprehensive registration dossier designed to demonstrate high similarity to a reference biological product. Due to the complexity of biological medicines, regulatory authorities require structured presentation of quality, non-clinical, and clinical data using internationally recognized or nationally defined dossier formats. These formats may include the Common Technical Document (CTD), the ASEAN Common Technical Dossier (ACTD), or country-specific checklist-based dossier systems. Although these dossier formats differ in structure and administrative requirements, they are all built on a common scientific foundation and support a comparability-based regulatory assessment.[8,9]

2.1 CTD-Based Dossier Systems

The Common Technical Document is an internationally harmonized dossier format primarily used in highly regulated markets. It is mandatory for biosimilar registration in the United States and is organized into five modules covering administrative, quality, non-clinical, and clinical information. The CTD framework allows regulators to systematically assess biosimilarity while accommodating regional administrative requirements through a dedicated administrative module.[4,9]

Table 2.1: US CTD Module 1 (Administrative and Prescribing Information).

SR. NO.		DOCUMENTS
1.0		Cover Letter
	1.0.1	Comprehensive Table of Contents (Modules 1–5)
	1.0.2	Module 1 Table of Contents
1.1		Administrative Information
	1.1.1	FDA Form 356h – Application to Market a New or Abbreviated Drug or Biologic
	1.1.2	Cover Sheet
	1.1.3	User Fee Cover Sheet (FDA Form 3397)
	1.1.4	Proof of User Fee Payment
	1.1.5	Applicant Contact Information
	1.1.6	Establishment Description
1.2		Application Information
	1.2.1	Applicant Information (Name and Address)
	1.2.2	Manufacturer Information (Drug Substance and Drug Product)
	1.2.3	Establishment Registration Number
	1.2.4	FEI Number (FDA Establishment Identifier)

	1.2.5	DUNS Number
1.3		Legal and Regulatory Information
	1.3.1	Letter of Authorization
	1.3.2	Power of Attorney
	1.3.3	Debarment Certification
	1.3.4	Financial Disclosure Certification (Form FDA 3454 or 3455)
	1.3.5	Patent Certification (Form FDA 3542, if applicable)
	1.3.6	Field Copy Certification
1.4		Reference Information
	1.4.1	Cross-Reference Authorization to Drug Master File (DMF)
	1.4.2	Cross-Reference Authorization to Master Files
	1.4.3	Reference Product Information (for Biosimilars)
1.5		Labelling
	1.5.1	Prescribing Information (Package Insert)
	1.5.2	Container Label
	1.5.3	Carton Label
	1.5.4	Patient Package Insert
	1.5.5	Medication Guide
	1.5.6	Instructions for Use
1.6		Risk Management
	1.6.1	Risk Evaluation and Mitigation Strategy (REMS), if applicable
	1.6.2	Pharmacovigilance Plan
	1.6.3	Risk Management Plan
1.7		Environmental Assessment
	1.7.1	Environmental Assessment Report
	1.7.2	Claim for Categorical Exclusion
1.8		Establishment and Manufacturing Information
	1.8.1	Establishment Registration Information
	1.8.2	GMP Certificates
	1.8.3	Manufacturing License
	1.8.4	Facility Information
1.9		Compliance Information
	1.9.1	Patent Information
	1.9.2	Exclusivity Information
	1.9.3	Orphan Drug Designation (if applicable)
1.10		Regional Information
	1.10.1	REMS Supporting Document
	1.10.2	Post Marketing Commitments
	1.10.3	Post Marketing Requirements

2.2 ASEAN Common Technical Dossier (ACTD)

The ASEAN Common Technical Dossier is a regional dossier format adopted by ASEAN member states, including the Philippines. ACTD is structured into four parts covering administrative, quality, non-clinical, and clinical documentation. While structurally different from CTD, ACTD requires similar scientific content for biosimilars and supports adaptation of CTD-based dossiers into ASEAN submissions with minimal scientific modification.[10,11]

Table 2. 2: Part I - Philippines Biosimilar Requirement.

SR. NO.	DOCUMENTS
Part I	Administrative Data and Product Information
A	Introduction
B	Overall ASEAN Common Technical Dossier Table of Contents
C	Guidance on Administrative Data and Product Information
1	Duly accomplished and notarized Integrated Application Form
2	Letter of Authorization
3	Relationship letter (between manufacturer and RTM / its affiliated companies)
4	Certificate of Pharmaceutical Product (COPP) – valid COPP (marketed and licensed from the country of origin) along with qualitative and quantitative composition – apostilled
5.1	License of pharmaceutical industries and contract manufacturer (For contract manufacturing)
5.2	Contract manufacturing agreement (For contract manufacturing)
5.3	GMP certificate of contract manufacturer – apostilled (For contract manufacturing)
6.1	License of pharmaceutical industries (For manufacturing under-license)
6.2	GMP certificate of manufacturer – apostilled (For manufacturing under-license)
6.3	Copy of under-license agreement
7.1	License of pharmaceutical industries (For locally manufactured products)
7.2	GMP certificate (country specific) – apostilled (For locally manufactured products)
8.1	License of pharmaceutical industries/importer/wholesaler (country specific)
8.2	Certificate of Pharmaceutical Product issued by competent authority in country of origin (WHO format)
9	Site Master File
10	Labelling / artwork in open/editable CDR file
11	Representative sample with corresponding Certificate of Analysis (upon evaluator request)
12.1	Package Insert – open/editable CDR file
12.2	Summary of Product Characteristics (Product Data Sheet)
13.1	Core / Global Risk Management Plan (RMP)
13.2	Philippine-Specific Risk Management Plan Annex
14	Periodic Safety Update Report (PSUR) / Periodic Benefit-Risk Evaluation Report (PBRER)
15	Name of medical director of importer/distributor and local manufacturer responsible for pharmacovigilance reporting
16	Person(s) responsible for production and quality control (Name, Position, Department, Signature specimen)
17	Description of cold-chain procedures from origin to port of entry and within Philippines
18	Lot/batch numbering system description
19	Reprocessing procedure for rejected lot/batch by QA/QC
20	Lot-to-lot consistency data from three consecutive batches

2.3 Country-Specific Checklist-Based Dossier Systems: The Colombian Model

Unlike the United States and ASEAN countries, Colombia does not mandate CTD or ACTD formats for biosimilar registration. Instead, the Colombian regulatory authority, INVIMA, applies a country-specific dossier structure supported by detailed regulatory checklists.[12,13]

Key features of the Colombian dossier system include

Submission of data according to national INVIMA requirements

Use of structured checklists for administrative, quality, non-clinical, and clinical evaluation

Acceptance of CTD-aligned scientific content, without requiring CTD formatting.

Table 2.3: Administrative and Legal Requirements for Colombia.

SR. No.	DOCUMENTS
	ADMINISTRATIVE DOCUMENTS (LOCAL)
1	Verify current pharmacological norms of INVIMA
2	Verify Local Data Protection compliance (Decree 2085)
3	Receipt of fee payment according to current INVIMA rate manual
4	Signed application letter
5	INVIMA application form according to current official version
6	General product information including brand name, active ingredient, dosage form, manufacturer, Marketing Authorization Holder (MAH), importer, local packager, regulatory modality, presentations, and shelf life
7	IUM (Código Único de Medicamento) for each presentation
	LEGAL DOCUMENTS
8	GMP certificate for finished product and intermediates, with official Spanish translation and apostilled, issued by competent authority from accepted countries (USA, Canada, EU countries, UK, Japan, Australia, WHO, PAHO, etc.)
9	GMP certificate for API, intermediates, bulk manufacturer, packaging site, and diluent manufacturer, with official translation and apostilled
10	Certificate of Pharmaceutical Product (CPP), issued by health authority of country of origin, with official translation and apostilled, including product composition, MAH, manufacturer, registration details, and GMP compliance certification
11	Copy of manufacturing agreement and packaging agreement (mandatory for local activities, if applicable)
12	Trademark certificate issued by Superintendency of Industry and Commerce; if trademark owner is a third party, include authorization letter
13	Authorization letter from manufacturer and/or product owner authorizing the Sanitary Registry holder to import, distribute, and sell the product in Colombia

2.4 Scientific Content Convergence Across Dossier Formats

Despite differences in dossier structure, CTD, ACTD, and Colombian national dossiers converge in their scientific expectations for biosimilars. All systems require:

- Extensive quality and analytical comparability data
- Risk-based non-clinical evaluation

- Targeted clinical studies where necessary
- Post-marketing pharmacovigilance commitments.

As a result, biosimilar developers commonly prepare a single core scientific dossier, which is then adapted into CTD, ACTD, or country-specific checklist formats depending on regulatory requirements.[1,8]

2.5 Practical Implications for Multi-Country Biosimilar Registration

The coexistence of CTD, ACTD, and national checklist-based dossier systems highlights the importance of strategic dossier planning. While administrative presentation varies, core quality documents such as specifications and Certificates of Analysis are often identical across submissions, supporting efficient reuse of data.[6] Core quality documents, including Certificates of Analysis and finished product specifications, are typically reused across multiple regulatory submissions and form part of the quality documentation supporting biosimilar registration. Representative examples of these documents are provided in the Supplementary Annexure.[8]

Table 2.4: Biosimilar Dossier Architecture Across Regulatory Systems (United States, Colombia, and Philippines)

Dossier Component	United States	Colombia	Philippines
Regulatory Authority	US FDA	INVIMA	FDA Philippines
Dossier Format Mandated	eCTD (Electronic Common Technical Document)	Country-specific national dossier	ASEAN Common Technical Dossier (ACTD)
Administrative Section	Module 1 (Region-specific)	National administrative requirements	ACTD Part I
Quality Documentation	Module 3 (Quality)	National quality checklist (CTD-aligned content)	ACTD Part II
Non-Clinical Data	Module 4	National non-clinical checklist	ACTD Part III
Clinical Data	Module 5	National clinical checklist	ACTD Part IV
Scientific Content Basis	Fully CTD-based	CTD-aligned, checklist-driven	CTD-aligned via ACTD
Electronic Submission	Mandatory	Optional / Hybrid	Partial / Country-dependent
Use of Regulatory Checklists	Limited (guidance-based review)	Extensive (INVIMA checklists)	Moderate (ASEAN + national checklists)
Reuse of Core	High	High	High

Scientific Data			
Adaptability for Multi-Country Submission	Moderate	High	High

2.6 SUMMARY

Biosimilar dossier formats vary across regulatory jurisdictions, ranging from CTD and ACTD to country-specific checklist-based systems. However, the underlying scientific principles governing biosimilar evaluation remain consistent.

REGULATORY PATHWAY FOR BIOSIMILAR PRODUCT REGISTRATION IN THE UNITED STATES

3. Introduction to the United States Regulatory System for Biosimilars

The United States represents one of the most advanced and highly regulated pharmaceutical markets globally. It was among the first countries to establish a dedicated legal and regulatory framework for biosimilar products, recognizing the scientific and regulatory differences between biosimilars and conventional generic drugs. The U.S. biosimilar regulatory system is characterized by a strong statutory foundation, extensive regulatory guidance, and a science-driven evaluation process based on analytical comparability and the totality-of-evidence concept.[14,15]

The U.S. approach to biosimilar regulation has played a significant role in shaping global regulatory practices and serves as a benchmark for biosimilar development strategies worldwide.[14]

3.1 Regulatory Authority Governing Biosimilar Products

Biosimilar products in the United States are regulated by the U.S. Food and Drug Administration (FDA). Within the FDA, responsibility for the review and approval of biosimilar products lies primarily with the Center for Drug Evaluation and Research (CDER) and, in certain cases, the Center for Biologics Evaluation and Research (CBER), depending on the nature of the biological product.[14,16]

The FDA is responsible for

- Evaluation of biosimilar applications
- Assessment of quality, non-clinical, and clinical comparability
- Inspection of manufacturing facilities

- Granting of biosimilar and interchangeability approvals
- Post-marketing surveillance and lifecycle oversight.

The FDA operates under a highly structured regulatory environment supported by detailed guidance documents that clarify regulatory expectations for biosimilar development.[15]

3.2 Legal Framework for Biosimilar Approval in the United States

The legal basis for biosimilar regulation in the United States is established under the Public Health Service Act, as amended by the Biologics Price Competition and Innovation Act (BPCIA). This legislation created a dedicated abbreviated approval pathway for biosimilar and interchangeable biological products. Under this framework, a biosimilar is defined as a biological product that is highly similar to a reference biological product, notwithstanding minor differences in clinically inactive components, and for which there are no clinically meaningful differences in terms of safety, purity, and potency.[17]

3.3 Dossier Format and Submission Requirements

Biosimilar applications in the United States must be submitted in the electronic Common Technical Document (eCTD) format. The eCTD provides a harmonized and standardized structure that supports efficient regulatory review and lifecycle management of biological products.[9,18]

The eCTD dossier is organized into five modules

- **Module 1:** Administrative and regional information
- **Module 2:** Summaries and overviews
- **Module 3:** Quality information, including manufacturing and analytical comparability data
- **Module 4:** Non-clinical study reports
- **Module 5:** Clinical study reports.

Among these modules, Module 3 (Quality) plays a central role in biosimilar evaluation, as the demonstration of analytical and functional similarity forms the foundation of regulatory decision-making.[4,9]

3.4 Regulatory Approval Pathway for Biosimilar Products in the United States

The U.S. biosimilar approval pathway follows a stepwise and structured regulatory process designed to establish biosimilarity through a totality-of-evidence approach. Each stage of development and evaluation builds upon the previous one, with the extent of data required determined by the degree of similarity demonstrated.[14,15]

Step 1: Selection of Reference Biological Product

The biosimilar development process begins with the selection of a U.S.-licensed reference biological product. The reference product must be approved in the United States, ensuring that biosimilarity is established against a product with a well-defined regulatory and clinical history.

Step 2: Analytical and Quality Comparability

Extensive analytical characterization is conducted to compare the proposed biosimilar with the reference product. This includes assessment of structural, physicochemical, and functional attributes, as well as evaluation of manufacturing process consistency and control strategies.

This step is considered the most critical phase of biosimilar development and largely determines the scope of subsequent non-clinical and clinical studies.

Step 3: Non-Clinical and Clinical Development

Based on analytical comparability outcomes, targeted non-clinical and clinical studies are designed to address any residual uncertainty. Clinical studies typically focus on pharmacokinetics, pharmacodynamics, and immunogenicity, with confirmatory efficacy studies conducted where necessary.

Step 4: Regulatory Interaction with the FDA

The FDA encourages early and ongoing interaction with biosimilar developers through scientific advice meetings. These interactions allow applicants to discuss development strategies, study designs, and regulatory expectations, thereby facilitating efficient review and reducing the likelihood of regulatory deficiencies.

Step 5: Submission of Biosimilar Application

The biosimilar application is submitted to the FDA in eCTD format under the designated biosimilar approval pathway. The submission includes comprehensive quality data,

comparative non-clinical and clinical evidence, and supporting summaries demonstrating biosimilarity.

Step 6: FDA Review and Manufacturing Site Inspection

The FDA conducts a detailed scientific review of the application and may perform inspections of manufacturing facilities to ensure compliance with applicable quality standards and good manufacturing practices.

Step 7: Regulatory Decision and Approval

Based on the totality of evidence, the FDA may approve the product as a biosimilar. In cases where additional evidence is provided, the product may also be granted an interchangeability designation, allowing substitution under specific regulatory conditions.

Step 8: Post-Approval Monitoring and Lifecycle Management

Following approval, manufacturers are required to implement pharmacovigilance systems, report adverse events, and manage post-approval changes in accordance with regulatory requirements to ensure ongoing product quality and patient safety.[5,15,16]

3.5 SUMMARY

The United States biosimilar regulatory pathway represents a highly structured, science-driven model with clear legal foundations and detailed regulatory guidance. Understanding this pathway provides a critical reference point for comparing biosimilar regulatory systems in other jurisdictions, including Colombia and the Philippines, which are discussed in subsequent sections.

REGULATORY PATHWAY FOR BIOSIMILAR PRODUCT REGISTRATION IN COLOMBIA

4. Introduction to the Colombian Regulatory System for Biosimilars

Colombia represents one of the most structured and progressive regulatory systems for biosimilar products in Latin America. Recognizing the importance of biosimilars in improving access to biological therapies, Colombia has established a specific national regulatory framework for biological and biosimilar products. Unlike some countries that rely solely on international dossier formats, Colombia follows a country-specific regulatory model supported by defined legal provisions and detailed evaluation checklists.

The Colombian biosimilar regulatory system is notable for its flexibility, risk-based evaluation approach, and alignment with international scientific principles while maintaining national regulatory autonomy.[19,20]

4.1 Regulatory Authority Governing Biosimilar Products

Biosimilar products in Colombia are regulated by the National Institute for Food and Drug Surveillance (Instituto Nacional de Vigilancia de Medicamentos y Alimentos – INVIMA). INVIMA is the national regulatory authority responsible for the evaluation, approval, and post-marketing surveillance of pharmaceutical and biological products in Colombia.

INVIMA's responsibilities in biosimilar regulation include

- Evaluation of registration applications for biological and biosimilar products
- Scientific assessment of quality, non-clinical, and clinical data
- Review using national regulatory checklists
- Inspection of manufacturing facilities and verification of GMP compliance
- Post-approval pharmacovigilance and lifecycle oversight

INVIMA operates under a centralized regulatory system with clearly defined procedures for biological products.[19,21]

4.2 Legal Framework for Biosimilar Approval in Colombia

The regulatory framework for biosimilar products in Colombia is established under Decree 1782 of 2014, which provides a dedicated legal basis for the registration of biological and biosimilar medicines. This decree formally distinguishes biosimilars from both originator biological products and conventional generics.

Decree 1782 defines biosimilars as biological products that demonstrate similarity to a reference biological product in terms of quality, safety, and efficacy, based on a comparability exercise. The decree establishes specific regulatory routes and requirements tailored to the nature of biological products.[19,20]

4.3 Dossier Format and Submission Requirements

Unlike the United States, Colombia does not mandate the use of CTD or eCTD formats for biosimilar submissions. Instead, INVIMA requires submission of a country-specific dossier structured according to national regulatory requirements and supported by detailed evaluation checklists.

Key characteristics of the Colombian dossier system include

- Nationally defined dossier structure
- Use of INVIMA-specific administrative and technical checklists
- Acceptance of scientific data presented in a CTD-aligned manner
- Flexibility in dossier presentation while maintaining scientific rigor.

Although the format is country-specific, the scientific content expected by INVIMA is broadly aligned with international biosimilar regulatory principles.[19,21]

4.4 Regulatory Approval Pathway for Biosimilar Products in Colombia

The biosimilar approval pathway in Colombia follows a structured, stepwise regulatory process, guided by national legislation and scientific comparability principles. The pathway allows INVIMA to evaluate biosimilars using a risk-based approach while ensuring patient safety and product quality.

Step 1: Selection of Reference Biological Product

The biosimilar development process begins with the selection of an appropriate reference biological product. Colombia allows the use of reference products approved either domestically or by recognized foreign regulatory authorities, subject to scientific justification. This flexibility supports global biosimilar development strategies and facilitates access to suitable comparator products.

Step 2: Quality and Analytical Comparability

Applicants are required to demonstrate similarity between the proposed biosimilar and the reference product through comprehensive analytical and quality studies. This includes evaluation of structural, physicochemical, and functional characteristics, as well as manufacturing process controls. Quality comparability forms the foundation of the Colombian biosimilar approval process and directly influences the extent of subsequent data requirements.

Step 3: Non-Clinical and Clinical Evaluation

Based on the outcomes of analytical comparability, targeted non-clinical and clinical studies are conducted to address residual uncertainty. The scope of these studies is determined on a

case-by-case basis and may be reduced when strong similarity is demonstrated at the quality level. Clinical evaluation focuses on confirming comparable safety, efficacy, and immunogenicity profiles.

Step 4: Submission of Biosimilar Application to INVIMA

The biosimilar application is submitted to INVIMA using the national dossier format, accompanied by completed regulatory checklists and supporting documentation. The submission includes administrative data, quality documentation, and comparative non-clinical and clinical evidence.

Step 5: Scientific Review and Regulatory Assessment

INVIMA conducts a comprehensive scientific review of the application using structured evaluation checklists. The review process assesses the completeness, consistency, and scientific validity of the submitted data. Manufacturing sites may be inspected to verify compliance with applicable quality standards.

Step 6: Regulatory Decision and Marketing Authorization

Following successful evaluation, INVIMA grants marketing authorization for the biosimilar product. Approval is based on the totality of evidence demonstrating similarity to the reference product and compliance with national regulatory requirements.

Step 7: Post-Approval Pharmacovigilance and Lifecycle Management

After approval, biosimilar manufacturers are required to implement pharmacovigilance systems, report adverse events, and manage post-approval changes in accordance with INVIMA regulations. Ongoing regulatory oversight ensures continued product quality and patient safety.[1,19,21]

4.5 SUMMARY

The Colombian biosimilar regulatory pathway represents a nationally defined, checklist-based regulatory model that combines international scientific principles with country-specific regulatory requirements. Its flexibility in reference product selection and data requirements makes it an important regulatory system for biosimilar development in Latin America and provides a valuable comparison with more structured CTD-based systems.

REGULATORY PATHWAY FOR BIOSIMILAR PRODUCT REGISTRATION IN THE PHILIPPINES

5. Introduction to the Philippine Regulatory System for Biosimilars

The Philippines has established a developing yet structured regulatory framework for the approval of biosimilar products, reflecting its commitment to improving access to biological therapies while ensuring patient safety. As a member of the Association of Southeast Asian Nations (ASEAN), the Philippine regulatory system integrates national pharmaceutical laws with regional harmonization initiatives.[22,23] The biosimilar regulatory pathway in the Philippines is characterized by the adoption of ASEAN Common Technical Dossier (ACTD) principles, increasing use of regulatory reliance, and alignment with international scientific standards for biosimilar evaluation.[10,22]

5.1 Regulatory Authority Governing Biosimilar Products

Biosimilar products in the Philippines are regulated by the Food and Drug Administration of the Philippines (FDA Philippines), which operates under the Department of Health (DOH). FDA Philippines is the national regulatory authority responsible for the evaluation, approval, and post-marketing surveillance of pharmaceutical and biological products.[22,24]

Key responsibilities of FDA Philippines in biosimilar regulation include

- Review and approval of biosimilar registration applications
- Scientific assessment of quality, non-clinical, and clinical data
- Evaluation of dossiers using ACTD format
- Inspection of manufacturing facilities and verification of GMP compliance
- Post-marketing pharmacovigilance and regulatory oversight.[22]

5.2 Legal Framework for Biosimilar Approval in the Philippines

The legal basis for the regulation of biosimilar products in the Philippines is established under Republic Act No. 9711, commonly known as the Food and Drug Administration Act of 2009. This Act provides FDA Philippines with the authority to regulate health products, including biological and biosimilar medicines.[23] Under this framework, biosimilars are regulated as biological products requiring demonstration of quality, safety, and efficacy through a comparability-based approach. Supplementary administrative orders and regulatory circulars further define the requirements for biological and biosimilar product registration.[22,23]

5.3 Dossier Format and Submission Requirements

The Philippines mandates the use of the ASEAN Common Technical Dossier (ACTD) format for pharmaceutical product registration, including biosimilars. The ACTD is a regionally harmonized dossier format designed to streamline submissions across ASEAN member states.[10,11]

The ACTD structure consists of four parts

Part I: Administrative data and product information

Part II: Quality documentation

Part III: Non-clinical documentation

Part IV: Clinical documentation

Although the ACTD differs structurally from the CTD, the scientific content required for biosimilar evaluation is closely aligned with international standards. CTD-based scientific data can therefore be adapted into ACTD format with minimal modification.[10]

5.4 Regulatory Approval Pathway for Biosimilar Products in the Philippines

The biosimilar approval pathway in the Philippines follows a structured, stepwise regulatory process based on scientific comparability and risk-based evaluation. FDA Philippines applies national regulatory requirements while considering international regulatory experience and, where appropriate, reliance on approvals by recognized regulatory authorities.[22,24]

Step 1: Selection of Reference Biological Product

The biosimilar development process begins with the selection of an appropriate reference biological product. FDA Philippines allows the use of reference products approved either locally or by recognized foreign regulatory authorities, provided that adequate justification and supporting data are submitted. This flexibility supports efficient biosimilar development and facilitates multi-country registration strategies.

Step 2: Quality and Analytical Comparability

Applicants must demonstrate similarity between the proposed biosimilar and the reference product through comprehensive analytical and quality studies. These studies evaluate structural, physicochemical, and functional attributes, as well as manufacturing process controls and product consistency. Quality comparability forms the cornerstone of biosimilar evaluation in the Philippines and directly influences the scope of non-clinical and clinical data requirements.

Step 3: Non-Clinical and Clinical Evaluation

Based on analytical comparability outcomes, targeted non-clinical and clinical studies are conducted to address residual uncertainty. Clinical evaluation typically focuses on pharmacokinetics, pharmacodynamics, and immunogenicity, with confirmatory efficacy studies conducted when necessary. The extent of non-clinical and clinical data is determined using a risk-based approach.

Step 4: Submission of Biosimilar Application to FDA Philippines

The biosimilar application is submitted to FDA Philippines in ACTD format, along with required administrative documentation, quality data, and comparative non-clinical and clinical evidence. The submission must comply with national regulatory requirements and ASEAN harmonization principles.

Step 5: Regulatory Review and Evaluation

FDA Philippines conducts a scientific review of the application to assess completeness, data quality, and comparability. The review process may include verification of manufacturing site compliance and evaluation of reliance information from recognized regulatory authorities, where applicable.

Step 6: Regulatory Decision and Marketing Authorization

Upon satisfactory evaluation, FDA Philippines grants marketing authorization for the biosimilar product. Approval is based on the totality of evidence demonstrating similarity to the reference product and compliance with applicable regulatory standards.

Step 7: Post-Approval Pharmacovigilance and Lifecycle Management

After approval, biosimilar manufacturers are required to implement pharmacovigilance systems, report adverse events, and manage post-approval changes in accordance with national regulatory requirements. Continuous monitoring ensures ongoing product safety and quality.[1,4,22-24]

5.5 SUMMARY

The Philippine biosimilar regulatory pathway represents a regionally harmonized, ACTD-based regulatory model that integrates national regulatory authority with ASEAN principles and international scientific standards. Its flexibility in reference product acceptance and increasing use of regulatory reliance make it a key regulatory system within Southeast Asia

and an important comparator to CTD-based and checklist-based biosimilar regulatory frameworks.

COMPARATIVE ANALYSIS OF BIOSIMILAR REGULATORY PATHWAYS IN THE UNITED STATES, COLOMBIA, AND THE PHILIPPINES

6. Introduction to Comparative Regulatory Analysis

Comparative analysis of biosimilar regulatory pathways is essential to understand how common scientific principles are implemented through different legal, procedural, and administrative frameworks. Although the United States, Colombia, and the Philippines operate under distinct regulatory systems, all three jurisdictions apply a comparability-based approach for biosimilar evaluation.[1,6] This section provides a structured comparison of key regulatory elements across the three jurisdictions to highlight areas of convergence, divergence, and practical regulatory implications.

6.1 Comparison of Regulatory Authorities and Legal Frameworks

- All three countries have clearly designated national regulatory authorities responsible for biosimilar oversight, supported by defined legal frameworks.
- The United States regulates biosimilars under a dedicated statutory pathway with explicit legal provisions distinguishing biosimilars from originator biologics and generics.[17]
- Colombia has established a national biosimilar framework through specific legislation, supported by regulatory decrees that define biosimilar approval routes.[19]
- The Philippines regulates biosimilars under a broader pharmaceutical law framework, supplemented by administrative orders and regulatory guidance.[22,23]

While the U.S. framework is highly prescriptive and statute-driven, Colombia and the Philippines apply more flexible, policy-based regulatory models that allow adaptation to public health priorities.[6,13]

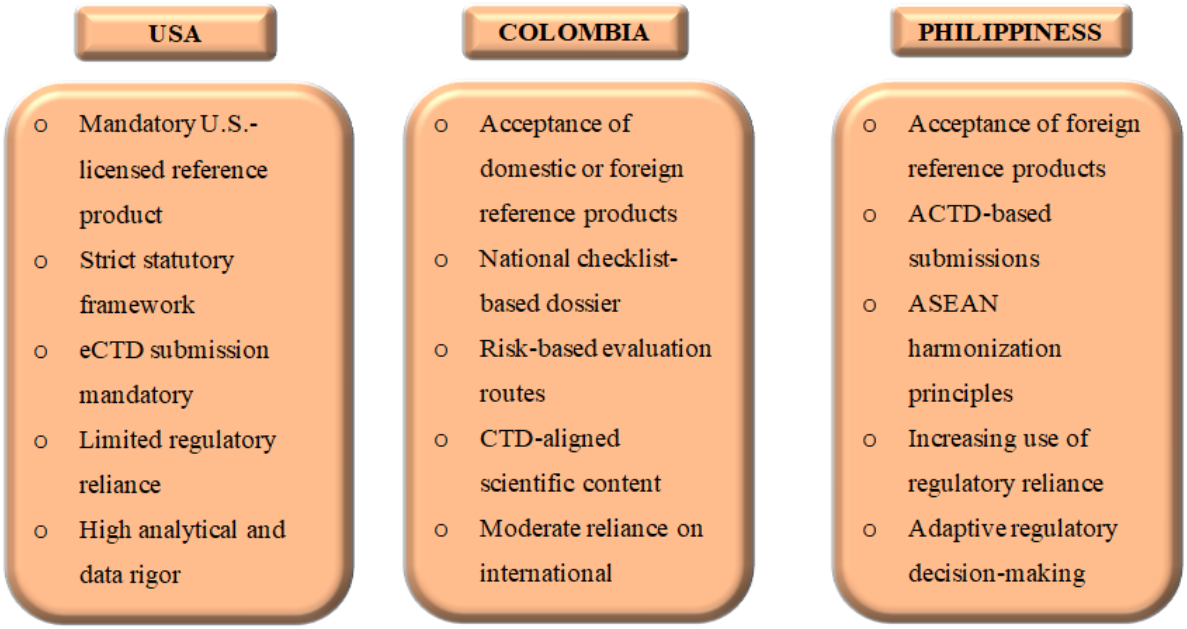

Figure 6.1: Comparative Regulatory Flexibility Spectrum for Biosimilar Registration

6.2 Comparison of Dossier Formats and Submission Systems.

Significant differences exist in dossier formats across the three jurisdictions

- The United States mandates submission in electronic Common Technical Document (eCTD) format.[9,18]
- Colombia requires a country-specific dossier, structured according to national requirements and evaluated using INVIMA checklists.[19,20]
- The Philippines mandates submission in ASEAN Common Technical Dossier (ACTD) format.[10,22]

Despite these structural differences, the scientific content expectations remain largely aligned, allowing biosimilar developers to prepare a single core scientific dossier and adapt it to each regulatory format.

6.3 Comparison of Reference Biological Product Requirements

Reference product selection represents a critical point of divergence

1) The United States requires the reference product to be licensed domestically.[17]

2) Colombia permits the use of reference products approved either domestically or by recognized foreign authorities.[19,20]

3) The Philippines allows reference products approved locally or by recognized foreign regulators, subject to justification.[22] Greater flexibility in reference product acceptance in

Colombia and the Philippines facilitates global biosimilar development, while the U.S. requirement introduces additional complexity and cost for manufacturers targeting the U.S. market.[13]

6.4 Comparison of Data Requirements and Evaluation Approach

All three jurisdictions apply a stepwise, totality-of-evidence approach, beginning with extensive analytical comparability and progressing to non-clinical and clinical evaluation as needed.

1) The United States applies the most rigorous analytical and scientific scrutiny, with limited regulatory flexibility.[14,15]
2) Colombia applies a risk-based approach that allows data reduction when strong similarity is demonstrated.[19,20]
3) The Philippines adopts a pragmatic evaluation model that balances scientific rigor with regulatory reliance.[22,24]

Although the extent of required data may vary, quality and analytical comparability remain the cornerstone of biosimilar evaluation in all three systems.

6.5 Comparison of Regulatory Approval Pathways

The regulatory approval pathways in the three countries share a common stepwise structure but differ in implementation:

1) The U.S. pathway is highly structured, with defined submission types, formal regulatory meetings, and detailed review processes.[14,15]
2) The Colombian pathway is checklist-driven, allowing structured evaluation while maintaining flexibility in data requirements.[19,20]
3) The Philippine pathway integrates ACTD-based review with reliance mechanisms to support efficient regulatory decision-making.[22,24]

These differences influence approval timelines, regulatory predictability, and submission strategies.

6.6 Comparison of Post-Approval Obligations and Pharmacovigilance

Post-approval oversight is a critical component of biosimilar regulation in all three jurisdictions.

1) The United States enforces stringent pharmacovigilance and lifecycle management requirements.[15]

2) Colombia requires post-marketing surveillance aligned with national pharmacovigilance systems.[19,21]
3) The Philippines mandates pharmacovigilance activities consistent with ASEAN and national safety monitoring frameworks.[22,24]

While the intensity of oversight varies, all three systems emphasize continued monitoring of biosimilar safety and quality throughout the product lifecycle.

6.7 Regulatory and Strategic Implications

The comparative analysis demonstrates that, despite structural and procedural differences, the three regulatory systems are converging toward common scientific principles for biosimilar evaluation. This convergence enables biosimilar developers to design global development strategies based on a unified scientific dossier while tailoring submissions to country-specific regulatory requirements.[8,13] Understanding these regulatory similarities and differences is critical for optimizing submission planning, minimizing regulatory risk, and accelerating market access across diverse jurisdictions.[6]

6.8 SUMMARY

The United States, Colombia, and the Philippines represent three distinct yet increasingly aligned biosimilar regulatory models. While the U.S. system emphasizes statutory rigor and scientific depth, Colombia and the Philippines demonstrate greater procedural flexibility through checklist-based and ACTD-based systems.

CHALLENGES IN MULTI-COUNTRY BIOSIMILAR REGISTRATION

7. Introduction to Regulatory and Developmental Challenges

Despite increasing global experience with biosimilar products and gradual convergence of regulatory principles, the registration of biosimilars across multiple countries remains complex and resource-intensive. These challenges arise from the inherent scientific complexity of biological products, combined with differences in regulatory frameworks, dossier formats, approval pathways, and post-approval requirements.[6,13]

Understanding these challenges is critical for pharmaceutical manufacturers, regulatory professionals, and policymakers involved in biosimilar development and global market access.

7.1 Scientific Complexity of Biosimilar Development

7.1.1 Analytical Variability and Critical Quality Attributes

Biological products exhibit inherent variability due to their complex molecular structure and sensitivity to manufacturing processes. Even minor changes in cell lines, raw materials, or process conditions can affect product quality. Identifying, controlling, and justifying critical quality attributes remains a major scientific challenge in biosimilar development. Regulatory authorities may differ in their interpretation of acceptable variability, leading to uncertainty during regulatory review across jurisdictions.[1,8]

7.1.2 Immunogenicity Assessment

Immunogenicity remains one of the most critical safety concerns associated with biosimilars. Differences in formulation, impurities, or manufacturing processes can influence immune responses. Designing sensitive immunogenicity studies and interpreting results across diverse populations present ongoing challenges, particularly in multi-country submissions.[4,5]

7.2 Regulatory Heterogeneity Across Jurisdictions

7.2.1 Differences in Legal and Regulatory Frameworks

Although biosimilars are recognized in all three jurisdictions, the legal and procedural frameworks differ significantly

1) The United States follows a highly structured, statute-driven regulatory model.[17]
2) Colombia applies a national, checklist-based system with defined regulatory routes.[19,20]
3) The Philippines integrates national regulations with ASEAN harmonization principles.[22,23]

These differences necessitate country-specific regulatory strategies, even when the scientific data package is largely identical.

7.2.2 Variability in Data Expectations

While all authorities adopt a comparability-based approach, expectations for non-clinical and clinical data may vary. Some jurisdictions allow reduced data packages when strong analytical similarity is demonstrated, whereas others require additional confirmatory studies. This variability can increase development costs and prolong approval timelines.[4,6]

7.3 Reference Product Selection Challenges

Reference product requirements differ across countries and represent a major challenge for global biosimilar development. The requirement for a domestically licensed reference product in certain jurisdictions complicates comparator sourcing and may necessitate additional bridging studies. In contrast, more flexible reference product acceptance in other markets introduces variability in regulatory expectations.[17,19,22]

7.4 Dossier Format and Administrative Challenges

7.4.1 Multiple Dossier Formats

Managing multiple dossier formats—eCTD for the United States, national checklist-based dossiers for Colombia, and ACTD for the Philippines—requires careful planning and coordination. Although scientific content can be reused, differences in structure, presentation, and administrative requirements increase the risk of inconsistencies and regulatory queries.[8,13]

7.4.2 Checklist-Based Review Complexity

Checklist-based evaluation systems, while structured, require meticulous alignment between submitted data and regulatory expectations. Minor administrative deficiencies can result in delays, additional queries, or rejection, even when scientific data are robust.[19,20]

7.5 Post-Approval and Lifecycle Management Challenges

Post-approval obligations represent a significant regulatory burden in multi-country biosimilar registration. Differences in pharmacovigilance requirements, adverse event reporting systems, and variation approval processes complicate global lifecycle management. Coordinating post-approval changes across jurisdictions while maintaining regulatory compliance remains a persistent challenge.[15,22,24]

7.6 Operational and Strategic Challenges

From an operational perspective, biosimilar developers must balance regulatory rigor with development efficiency. Challenges include

- Managing regulatory timelines across countries
- Coordinating regulatory interactions with multiple authorities
- Aligning global development strategies with local requirements.

In emerging regulatory systems, evolving guidelines and limited regulatory experience may further increase uncertainty.[6,13]

7.7 SUMMARY

The challenges associated with multi-country biosimilar registration are multifaceted, encompassing scientific complexity, regulatory heterogeneity, administrative burden, and lifecycle management issues. Addressing these challenges requires early regulatory planning, strong quality systems, effective dossier management, and continuous regulatory intelligence. These considerations highlight the need for greater regulatory harmonization and reliance mechanisms, which are discussed in the following section.

8. SAMPLE DOCUMENTS PREPARED FOR REGISTRATION PURPOSE

1) Finished Product Specifications: (3.2.P.5.1)

No.	Parameters	Method	Specification
1	Physical Appearance	Visual Inspection	Colourless to Slightly Yellow Solution
2	pH	pH Meter	5.0 – 5.5
Quantity			
3	Protein Concentration	UV Spectrophotometry	70.0 – 80.0 mg/mL
Primary Identity and Purity			
4	Receptor Binding Assay	ELISA	80.0 – 125.0% of Reference Standard
5	Peptide Mapping	RP-HPLC	Comparable with Reference Standard
6	Glycan Mapping	HILIC-UPLC	Sum of all Oligosaccharides with Galactose (G1, G1F, G2F) NMT 38.0%
7	High Molecular Weight Impurities	SE-HPLC	Main Peak: NLT 98.5%; Total Impurities: NMT 1.5%
8	Molecular Size & Integrity	SDS-PAGE (Coomassie Staining)	Reduced: Two Principal Bands of ~25 kDa and ~50 kDa Corresponding to Reference Standard. Non-Reduced: Dense Band of ~150 kDa Corresponding to Reference Standard
9	Size Heterogeneity	CE-SDS	Reduced: Sum of Heavy Chains and Light Chains ≥ 96.0%; Non-Reduced: Main Peak ≥ 65.0%
10	Isoelectric Point	cIEF	8.1 – 8.7
11	Charged Variants	IEX-HPLC	Acidic Charge Variants: NMT 10.0%; Main Peak: NLT 65.0%; Basic Charge Variants: NMT 30.0%
12	Host Cell DNA	q-PCR	NMT 10 ng/final Dose
13	Host Cell	ELISA	NMT 10.0 ppm

	Protein		
14	Residual Protein A	ELISA	NMT 10.0 ppm
15	Residual pDADMAC	SE-UPLC-ELSD	NMT 3 ppm
Safety			
16	Bacterial Endotoxins	LAL Test	NMT 0.08 EU/mg
17	Microbial Count	Microbial Limit Test	NMT 1 CFU/mL
Assay / Potency			
18	Potency	SEAP Reporter Gene Assay	80.0 – 125.0% of Reference Standard
		Prepared by	**Reviewed by**	**Approved by**
Name				
Signature				

2) Batch Analysis (3.2.P.5.4) – Certificate of Analysis of 3 Batches.

Product Name		Denosumab Pre-filled Syringe		**Manufacturing Date**		Dec 2022
Batch Numbers		FP011106, FP011107, FP011108		**Expiry Date**		Nov 2024
AR No.		AR/DS/2022/118		**Shelf Life**		36 Months
Batch Scale		14784, 15898, 16240 Pre-filled Syringes		**Storage Condition**		Store at 5±3°C
Batch Type		Commercial Scale Validation Batches		**Manufacturing Site**		
DS Batch No.		DS011106, DS011107, DS011108		**Strength**		60 mg/mL
No.	**Parameters**	**Method**	**Specification**	**FP011106**	**FP011107**	**FP011108**
1	Physical Appearance	Visual Inspection USP <790>, EP (2.2.1), EP (2.2.2)	Clear to Almost Clear, Colourless to Slightly Yellow Solution (≤ Y5 of EP)	Clear, Colourless	Clear, Colourless	Clear, Colourless
2	pH	pH Meter USP <791>, EP (2.2.3)	5.0 – 5.6	5.1	5.2	5.2
3	Extractable Volume	Volumetry USP <697>, EP (2.9.17)	1.00 – 1.03 mL	1.02 mL	1.02 mL	1.01 mL
4	Particulate Matter	Liquid Particle Counting USP <787>, EP (2.9.19)	10 µm ≤ 6000 Particles/Container; 25 µm ≤ 600 Particles/Container	10 µm: 20; 25 µm: 0	10 µm: 894; 25 µm: 2	10 µm: 512; 25 µm: 0
5	Osmolality	Osmometry USP <785>, EP (2.2.35)	320 ± 20 mOsmol/kg	336	325	326
6	Protein Concentration	UV Spectrophotometry (Internal Method)	55.0 – 65.0 mg/mL	58.2	61.6	59.5
7	Polysorbate 20	MM-HPLC (Internal Method)	0.06 – 0.15 mg/mL	N.T	N.T	N.T
8	Receptor	ELISA (Internal	80.0 – 125.0% of	102.0%	102.0%	96.0%

	Binding Assay	Method)	Reference Standard			
9	High Molecular Weight Impurities	SE-HPLC (Internal Method)	Total Impurities: NMT 1.8%	0.3%	0.4%	0.5%
10	Molecular Size & Integrity	SDS-PAGE (Coomassie Staining) (Internal Method)	Comparable to Reference Standard	Comparable to RS	Comparable to RS	Comparable to RS
11	Size Heterogeneity	CE-SDS (Internal Method)	Reduced: Sum of Heavy & Light Chains ≥96.0%; Non-Reduced: Main Peak ≥65.0%	N.T	N.T	N.T
12	Charged Variants	IEX-HPLC (Internal Method)	Main Peak: NLT 65.0%; Acidic Variants: NMT 10.0%; Basic Variants: NMT 30.0%	Main: 77.8%; Acidic: 3.9%; Basic: 18.3%	Main: 86.7%; Acidic: 2.8%; Basic: 10.5%	Main: 81.3%; Acidic: 6.3%; Basic: 12.3%
13	Isoelectric Point	cIEF (Internal Method)	8.1 – 8.7	8.3	8.3	8.3
14	Bacterial Endotoxins	LAL Test USP <85>, EP (2.6.14)	NMT 0.08 EU/mg	< 0.08 EU/mg	< 0.08 EU/mg	< 0.08 EU/mg
15	Sterility	Sterility Test USP <71>, EP (2.6.1)	Complies with Test for Sterility	Complies	Complies	Complies
16	Potency	Anti-differentiation Assay (Internal Method)	80.0 – 125.0% Reference Standard	108.4%	105.0%	96.5%
		Prepared By	**Reviewed By**		**Approved By**	
Name						
Signature						

3) Long Term Stability Report (3.2.P.8.3):

Product Name: Denosumab Prefilled Syringe 60 mg/ml									
Batch No.	FP011106		**Batch Size**			14784 Syringes			
Batch Type	Commercial Scale Batch		**Duration of Study**			36 Months			
Stability Study	Long Term Stability Study (5 ± 3°C)		**Manufacturing Date**			Sep 2022			
		Test Time Point (Month)							
Parameters	**Specifications**	**0**	**3**	**6**	**9**	**12**	**18**	**24**	**36**
Physical Appearance	Clear to Almost Clear, Colourless to Slightly Yellow Solution (≤ Y5 of EP)								
pH	5.0 – 5.6								

Extractable Volume	1.00 – 1.03 mL								
Particulate Matter	10 µm ≤ 6000 Particles/Container; 25 µm ≤ 600 Particles/Container								
Osmolality	320 ± 20 mOsmol/kg								
Protein Concentration	55.0 – 65.0 mg/mL								
Polysorbate 20	0.06 – 0.15 mg/mL								
Receptor Binding Assay	80.0 – 125.0% of Reference Standard								
High Molecular Weight Impurities	Total Impurities: NMT 1.8%								
Molecular Size & Integrity	Comparable to Reference Standard								
Size Heterogeneity	Reduced: Sum of Heavy & Light Chains ≥96.0%; Non-Reduced: Main Peak ≥65.0%								
Charged Variants	Main Peak: NLT 65.0%; Acidic Variants: NMT 10.0%; Basic Variants: NMT 30.0%								
Isoelectric Point	8.1 – 8.7								
Bacterial Endotoxins	NMT 0.08 EU/mg								

	Prepared by	**Reviewed by**	**Approved by**
Name			
Signature			

4) Accelerated Stability Report (3.2.P.8.3)

Product Name: Denosumab Prefilled Syringe 60 mg/ml			
Batch No.	FP011106	**Batch Size**	14784 Syringes
Batch Type	Commercial Scale Batch	**Duration of Study**	06 Months
Stability Study	Accelerated Stability Study (30 °C ± 2 °C / 65% ±5% RH)	**Manufacturing Date**	Sep 2022

		Test Time Point (Month)				
Parameters	**Specifications**	**0**	**1**	**2**	**3**	**6**
Physical Appearance	Clear to Almost Clear, Colourless to Slightly Yellow Solution (≤ Y5 of EP)					
pH	5.0 – 5.6					
Extractable Volume	1.00 – 1.03 mL					
Particulate Matter	10 µm ≤ 6000 Particles/Container; 25 µm ≤ 600 Particles/Container					

Osmolality	320 ± 20 mOsmol/kg					
Protein Concentration	55.0 – 65.0 mg/mL					
Polysorbate 20	0.06 – 0.15 mg/mL					
Receptor Binding Assay	80.0 – 125.0% of Reference Standard					
High Molecular Weight Impurities	Total Impurities: NMT 1.8%					
Molecular Size & Integrity	Comparable to Reference Standard					
Size Heterogeneity	Reduced: Sum of Heavy & Light Chains ≥96.0%; Non-Reduced: Main Peak ≥65.0%					
Charged Variants	Main Peak: NLT 65.0%; Acidic Variants: NMT 10.0%; Basic Variants: NMT 30.0%					
Isoelectric Point	8.1 – 8.7					
Bacterial Endotoxins	NMT 0.08 EU/mg					
	Prepared by	**Reviewed by**		**Approved by**		
Name						
Signature						

Note: The Above Prepare documents are for Reference use and they are not the real values, they are solely based on Pharmacopoeias.

CONCLUSION

Biosimilars represent a critical strategy for improving patient access to high-cost biological therapies while maintaining rigorous standards of quality, safety, and efficacy. This review provides a comprehensive comparative evaluation of biosimilar regulatory pathways in the United States, Colombia, and the Philippines, highlighting how common scientific principles are implemented through distinct legal, procedural, and administrative frameworks. The analysis demonstrates that all three jurisdictions adopt a comparability-based, stepwise evaluation approach centred on analytical similarity and the totality-of-evidence concept. However, meaningful differences exist in dossier formats, reference product requirements, regulatory flexibility, and reliance mechanisms. The United States follows a highly structured, statute-driven CTD-based system, whereas Colombia employs a national checklist-based regulatory model, and the Philippines integrates ACTD format with regional harmonization and reliance approaches.

Despite these differences, increasing convergence in scientific expectations and regulatory practices is evident. This convergence enables the development of unified biosimilar development strategies supported by adaptable dossier architectures. Continued regulatory harmonization, expanded use of reliance mechanisms, and strengthening of post-marketing surveillance systems are expected to further streamline biosimilar registration and lifecycle management. Overall, understanding both the similarities and distinctions among these regulatory systems is essential for regulators, industry professionals, and policymakers to optimize biosimilar development, facilitate efficient multi-country registration, and support sustainable healthcare systems globally.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest related to this work.

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