PERÚ | Ministerio de Salud | Viceministerio de Salud Pública | Dirección General de Medicamentos, Insumos y Drogas

GENERAL DIRECTORATE OF MEDICINES SUPPLYS AND DRUGS

Pharmaceuticals Product Directorate

Upcoming CMC Strategy Forum Latin America: CMC Conversations - CASSS

Changes post approval of biological products in Perú: Regulation and challenges

Pharm. Cinthia Noemi Torres Huari
Evaluator of the biological medicines products
DIGEMID, Perú

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BICENTENARIO DEL PERÚ 2021 - 2024

DIGEMID

-Line organ of the Ministry of Health, created with L.D. No. 584 of April 18, 1990.

-National authority for pharmaceutical products, medical devices and health products referenced in Law 29459.

-Certified in ISO 9001 Quality Managment and ISO 37001 Antibrybery.

SCOPE AND ORGANIZATION

PHARMACEUTICALS PRODUCTS DIRECTORATE	•Medicines, Natural, Dietetic And Others •Biological Products •Controlled Products
MEDICAL DEVICES AND SANITARY PRODUCTS DIRECTORATE	• Medical Devices • Sanitary Products
INSPECTION AND CERTIFICATION DIRECTORATE	• Warehouses and Stakeholders • Manufacturers • Control And Surveillance of Products • Illegal Trade
PHARMACOVIGILANCE, ACCESS AND USE DIRECTORATE	• Access To Medicines • Rational Use • National Center of Pharmacovigilance And Technovigilance

ROF S.D. No. 007-2016-SA and L.D. No. 1161 - LOF MINSA

ORGANIZATION OF THE REGULATORY FRAMEWORK FOR CHANGES POST APPROVAL OF BIOLOGICAL PRODUCTS

LAW

- Law 29459 : Sanitary Registry (SR) and Conditional Sanitary Registry (CSR)
  Art. 14.- Updating Sanitary Registry (SR)

REGULATION

- Supreme Decre: 016-2011-SA and amendments (Sanitary Registry)
  Art. 36° Pharmaceutical product changes
- Supreme Decre: 011-2016-SA (Biotecnological products)
- Supreme Decre: 011-2016-SA (Biosimilar products)
- Ministerial Resolution N° 893-2019/MINSA : Major changes in pharmaceutical products with health registration
- Supreme Decre: 002-2021-SA and amendments (Conditional Sanitary Registry)
- Supreme Decre: 020-2021-SA (Vaccines)
- Supreme Decre: 011-2023-SA (Other Biological products)-Valid until november

in Review

Pending:

- *Plasma and blood derived products*
- *Allergens*
- *Serums*

ROUTES OF AUTHORIZATION

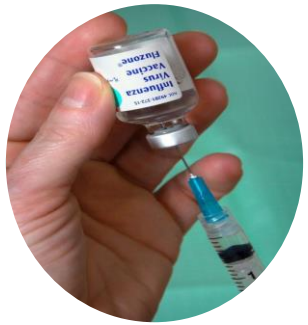
	SANITARY REGISTRY	CONDITIONAL SANITARY REGISTRY
VALIDITY	5 years and renewable.	1 year and renewable up to 4 times
SCOPE	Pharmaceuticals, medical devices and Health Products (NSO) with complete data (*).	Medicines and biological products with fase III in course
MANUFACTURE	1 Manufacturer and country	> 1 manufacturer /country
POST APPROVAL	Post registration changes	Post registration changes and specific obligations

(*) Orphan drugs in HSC phase II in course is acceptable with annual obligations

BIOLOGICAL PRODUCTS

IMMUNOLOGICAL

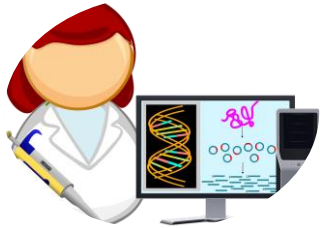
vaccines, allerges and serums



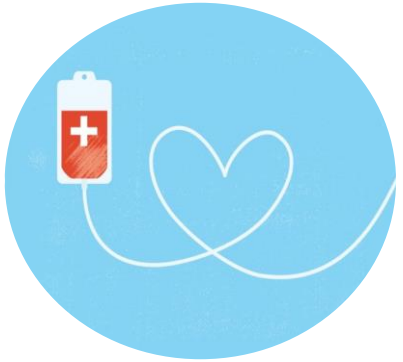
BIOTECHNOLOGICAL PRODUCTS

DNA Recombinant techniques

- Monoclonal antibody and hybridoma techniques
- Other methods determinate by the ANM in accordance to the advance of science



DERIVED FROM HUMAN BLOOD AND HUMAN PLASMA

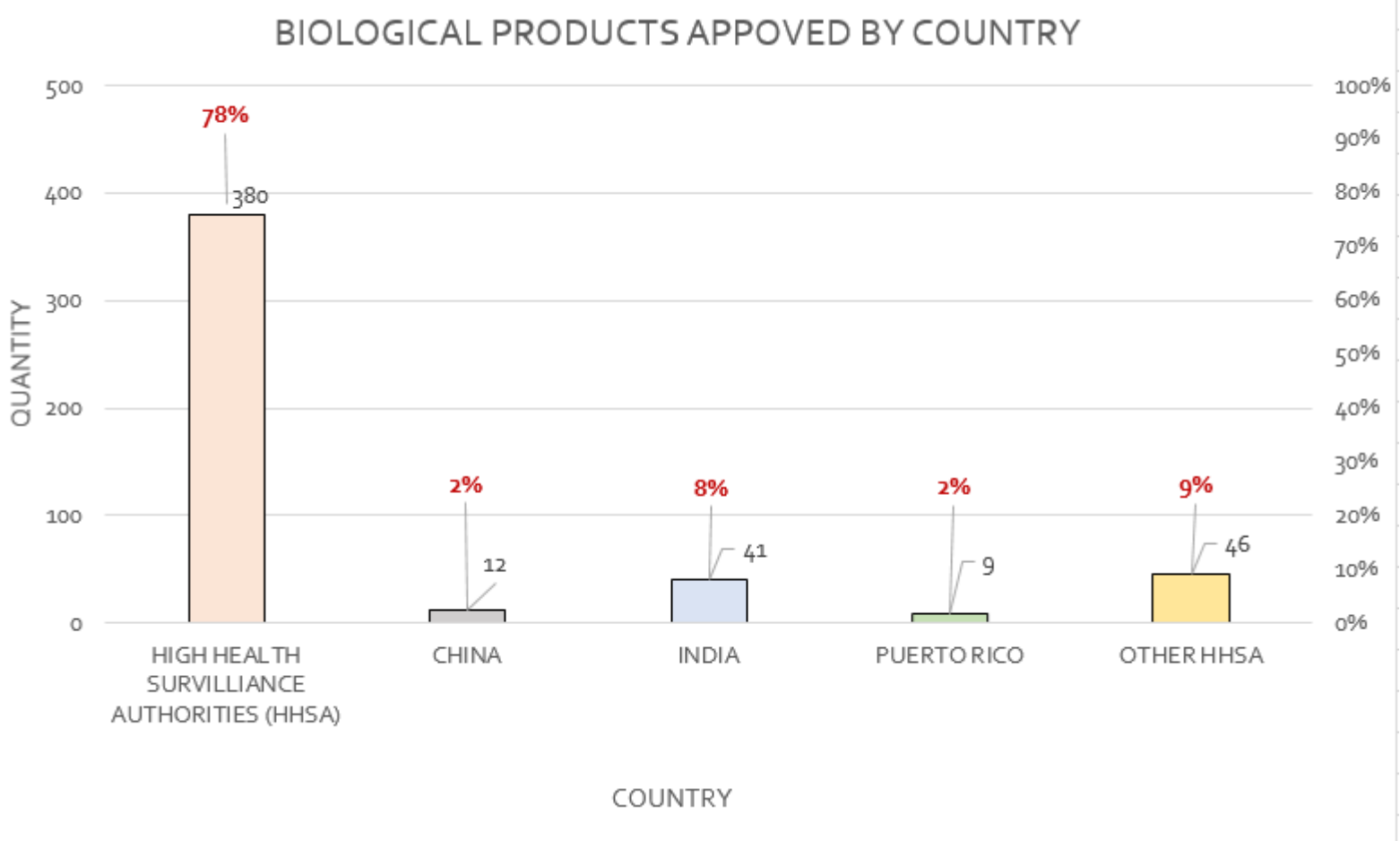


OTHER BIOLOGICAL PRODUCTS

ADVANCE THERAPIES

Legal Requirements CMC of API and finished product.	RMP Preclinical and clinical studies.	CTD Format Module 3,4 and 5 in english	Biosimilar applications	International Recommendations	Reduce time evaluation for specific products approved in HSC/EMA/WHO (180 days)

BIOLOGICAL PRODUCTS APPROVED



RESULT

488 BIOLOGICAL PRODUCTS APPROVED UNTIL AUGUST 2023

396 approved with CTD
66 in renewal
24 authorized for health interventions (international cooperation organizations)

HIGH HEALTH SURVILLIANCE AUTHORITIES

-**264** products are from EMA
-**57** products are from the United States

CLASSIFICATION OF CHANGES

TIPE	DESCRIPTION	ASSESSMENT DEADLINES
Changes of minor importance	Changes that have minimal or no impact on the Quality, safety or effectiveness.	**Automatic "communications format"(*)**
Changes of major importance	Changes that may have significant impacts on Quality, safety or effectiveness	**60 days**

Change of manufacturer of API and Finished Product (SCR)	Manufacturing process change	Change in the shelf life	Change in packaging material	Change of technical specifications	Change of labeling

Minor or major change case by case

(*) Changes not included in communications format are evaluate

INTERNATIONAL RECOMENDATIONS

PAHO RED PARF

World Health Organization

EUROPEAN MEDICINES AGENCY

FDA U.S. FOOD & DRUG ADMINISTRATION

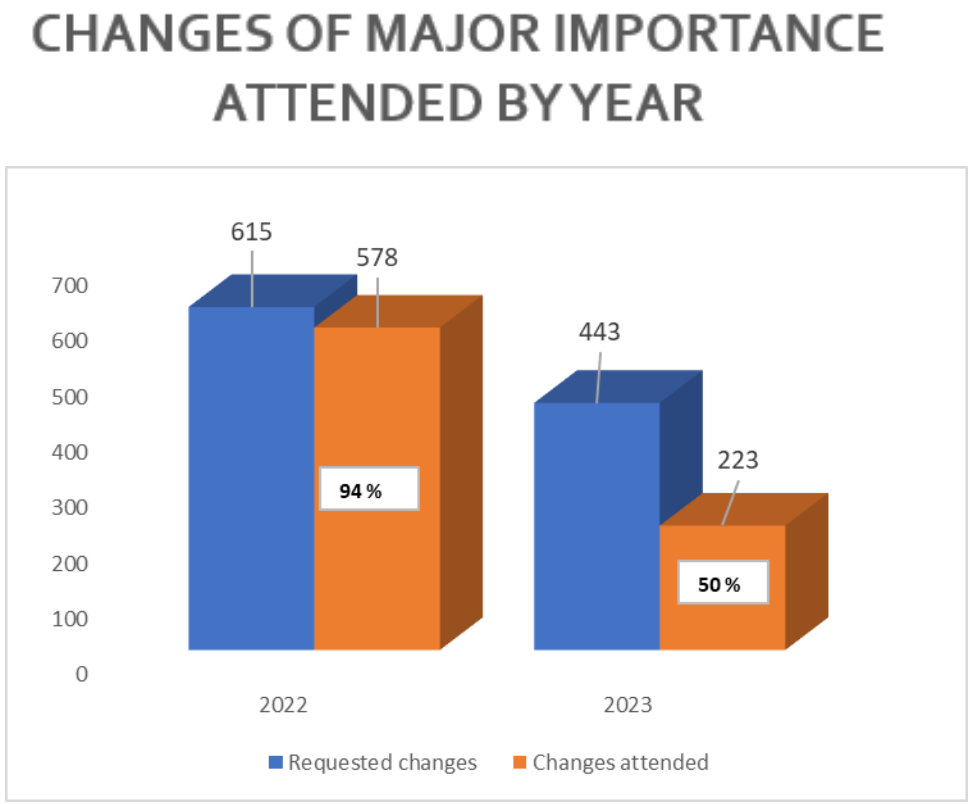
Health Canada

ICH

Vaccines, Biotechnological products, Biosimilar

Other biological products

CHANGES ATTENDED OF BIOLOGICAL PRODUCTS



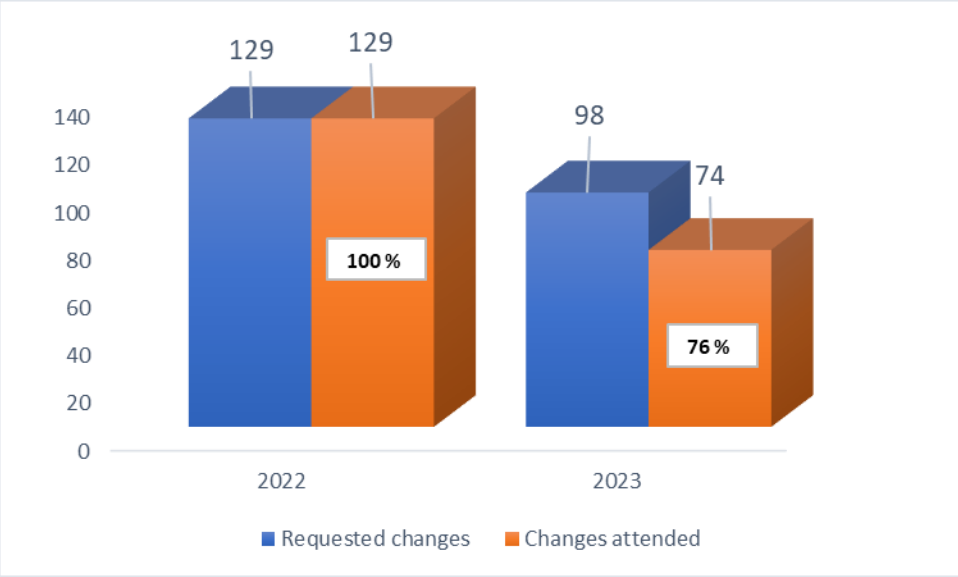
RESULT

-In 2022, 94% of the total changes were attended

- In 2023 there is progress of 50%

CHANGES ATTENDED OF BIOLOGICAL PRODUCTS

CHANGES OF MINOR IMPORTANCE ATTENDED BY YEAR



RESULT

-In 2022, 100% of the total changes were attended

- In 2023 there is progress of 76%

ACTIONS TO ADDRESS CHANGES POST APPROVAL APPLICATIONS

- Hiring human resources for the evaluation of changes
- Meetings of orientation to Marketing Authorization Holder (MAH).
- Prioritization of changes related to batch release, re-registrations, conditional sanitary registry
- Assignment of changes related to the same product or types of products to the same reviewer
- Regular communication with MAH during the evaluation of applications

CHALLENGES ADDOPTING WHO GUIDELINES

Differences in the classification of changes in DIGEMID, EMA and WHO

DIGEMID - PERÚ	OMS	EMA
Minor	Minor	Type IA (Minor)
Mayor	Moderate	Tipo IB (Moderate)
	Major	Tipo II (Major)

Requirements in the law of general administrative procedure and regulatory quality analysis that make it difficult to adopt the WHO guidelines

Description and composition of the drug product: change to a diluent

Description of change	Conditions to be fulfilled	Supporting data	Reporting category
36. Change to the diluent, involving the following:			
a. Change in manufacturing process	None	1–5	Moderate
	1, 3	1–4	Minor
b. Replacement of or addition to the source of a diluent	None	1–6	Moderate
	1–3	1–3	Minor
c. Change in facility used to manufacture a diluent (same company)	1, 2	1, 3, 5	Minor
d. Addition of a diluent filling line	1, 2, 4	1, 3, 5	Minor
e. Deletion of a diluent	None	None	Minor

Conditions

1. The diluent is water for injection or a salt solution (including buffered salt solutions) – that is, it does not include an ingredient with a functional activity such as a preservative, and there is no change to its composition.
2. After reconstitution, there is no change in the drug product specification outside the approved limits.
3. The proposed diluent is commercially available in the country/jurisdiction of the NRA.
4. The addition of the diluent filling line is in an approved filling facility.

Supporting data

1. Flow diagram (including process and in-process controls) of the proposed manufacturing process(es) and a brief narrative description of the proposed manufacturing process(es).
2. Updated copy of the proposed specification for the diluent.
3. Description of the batches and summary of results as quantitative data, in a comparative tabular format, for at least three consecutive commercial-scale batches of the approved and proposed diluent. Comparative test results for the approved diluent do not need to be generated concurrently; relevant historical testing results are acceptable.
4. Updated stability data on the product reconstituted with the new diluent.
5. Evidence that the facility is GMP-compliant.
6. Revised drug product labelling information, as applicable.

"Supporting data (requeriments) depends on description and conditions"

CHALLENGES IN THE EVALUATION OF POST APPROVAL CHANGES

- There is no specific regulation for description and specific requeriments of post-registration changes
- We are finalizing a regulatory transition that involves the registration of biological products with CTD format
- Regular meetings with Marketing Authorization holders due to observations in applications.
- Companies don't submit the same documentation with which the change was authorized in HHSA.
- Most of the Human Resources are allocated to the evaluation of the Registration and Re-registration processes

PERSPECTIVES

- Modification of our regulation with a view to regulatory convergence.
- Improve the capability of human resources with the cooperation of agencies with more experience.
- Incorporate reliance procedures for products approved in HHSA (attention to requests in less time).
- Facilitate information related to recognition through digital resources.
- 100% of Biological products approved with CTD
- Provide orientation to MAH in webinars, meeting, etc.

THANK YOU!
Muchas gracias!

Inquires/Questions:
http://www.digemid.minsa.gob.pe
ctorresh@minsa.gob.pe