REGULATION OF BIOLOGICAL PRODUCTS IN PERU

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CONTENTS

- Introduction of DIGEMID
- Legal Bases of Biological Products in Peru
- Biological Products authorized in Peru

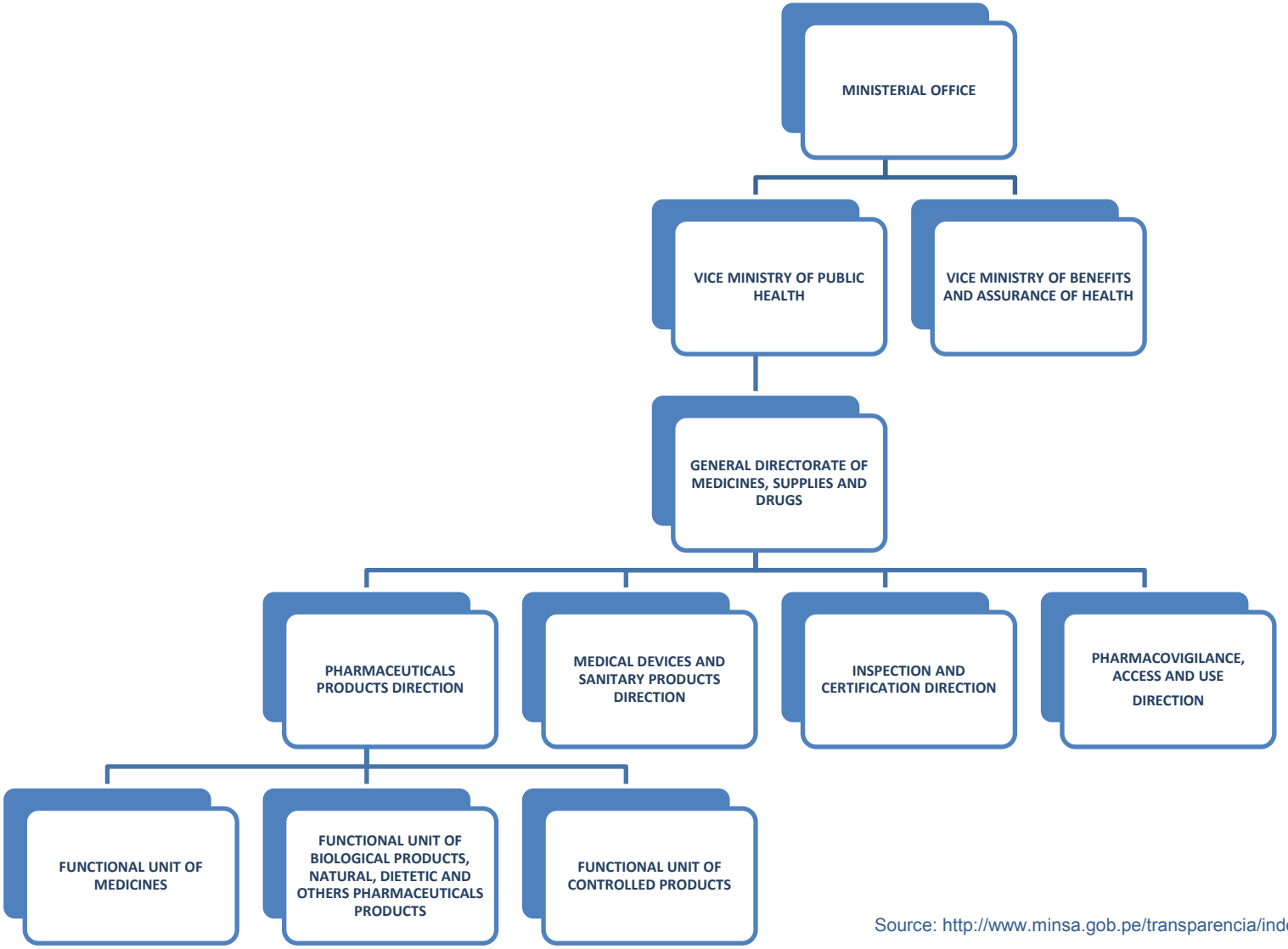
GENERAL DIRECTORATE OF MEDICINES, SUPPLIES AND DRUGS (DIGEMID)

- DIGEMID is a line organ of the Ministry of Health, created with Legislative Decree No. 584 of April 18, 1990 .
- DIGEMID is located in Lima, Perú.
- The main objective of DIGEMID is to ensure that the population has access to safe, effective and quality medicines, and that they are used rationally.

Source: http://www.digemid.minsa.gob.pe/

DIGEMID STRUCTURE

(according ROF S.D. No. 008-2017-SA and amendments and L.D. No. 1161 - LOF MINSA)



Source: http://www.minsa.gob.pe/transparencia/index.asp?op=115

Legal Bases of Biological Products in Perú

Law 29459, in 2009

Law of Pharmaceutical, Medical Devices and Health Products

Supreme Decree 016-2011 S.A. and amendments

Registration, Control and Health Surveillance of Pharmaceutical Products, Medical Devices and Health Products

Supreme Decree N° 011-2016-SA

Registration and re-registration of biotechnological products, also change the definition and clasification of biological products

Supreme Decree N° 013-2016-SA

Registration and re-registration of biological products that choose the similarity pathway

Source: http://www.digemid.minsa.gob.pe/

Law N° 29459
Law of pharmaceutical products, medical devices and sanitary products

- Issued in November 26th, 2009
- It establishes new requirements to approve pharmaceutical products and medical devices.
- "Pharmaceutical products" includes Biological products.
- It establishes principles to evaluate quality, efficacy and safety.

Source: http://www.digemid.minsa.gob.pe

Supreme Decree N° 016-2011-SA and amendments
Chapter V. Biological Products

- In Force in January 23th, 2011.

- Introduce:
  - Specific aspects of Law N° 29459.
  - New Definition and classification for biological products.
  - General requirements for the registration and re-registration biological products: full data of quality, efficacy and safety.
  - General requirements to submit and evaluate similar biological products: based on WHO recommendations.

Source: http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/DS016-2011-MINSA.pdf

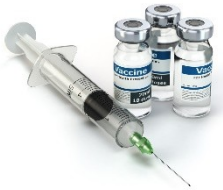
Regulatory change based on the Supreme Decree N° 016-2011-SA

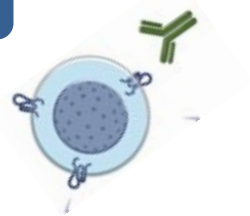
S.D. 010-1997-SA	S.D. 016-2011-SA
❑ No differences between requirements for the registration of chemical products and biological products.	❑ Specific requirements for biological products.
❑ Some data of quality, no evidence of efficacy and safety.	❑ Complete data of quality, efficacy and safety.
❑ Evaluation time: 60 days.	❑ Evaluation time: Vaccines and immunological products shall not exceed 180 calendar days. Rest of biological products is up to 12 months.

Source: http://www.digemid.minsa.gob.pe

BIOLOGICAL PRODUCTS (S.D. N° 016-2011-SA)

A biological product has a substance produced or extracted by a biological source and that needs for its characterization and determination of quality, a combination of physico-chemical and biological assays, along with the process of production and control





- Immunological (vaccines, allergens and serums)
- Blood and plasma derived products
- BIOLOGICAL PRODUCTS
- Biotechnological Products
- Other biological products

Source: http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/DS016-2011-MINSA.pdf

N°	REQUIREMENTS FOR THE REGISTRATION AND RE-REGISTRATION OF BIOLOGICAL PRODUCTS
1	Application form (Affidavit)
2	Quality control documentation (API, finished product, excipients)
3	Certificate of batch release
4	Standards and reference material documentation (API, finished product)
5	Manufacturing process description and its validation (API, finished product)
6	Stability studies
7	Certificate of Pharmaceutical Product
8	Good Manufacture Practice Certificate
9	Container closure system
10	Characterization of API and pharmaceutical development of finished product
11	Technical sheet and package insert
12	Project of labeling of mediate and immediate packages
13	Pre clinical studies
14	Clinical studies
15	Risk planning management

SIMILAR BIOLOGICAL PRODUCT - SBP
S. D. 016-2011-SA

- Biological products can apply for registration through **similarity pathway.**
- Documentation should supports comparability of quality between the similar biological product with the reference one.
- Requirements are those established in article 104° of the regulation. Requirements 13th and 14th are going to be replaced by pre-clinical and clinical studies that demonstrate efficacy and safety comparability between the SBP and the reference one.

Source: http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/DS016-2011-MINSA.pdf

SPECIFIC REGULATIONS:

REGULATION ABOUT THE SUBMISSION AND CONTENT OF THE DOCUMENTS REQUIRED FOR THE SANITARY REGISTRATION AND RE-REGISTRATION OF BIOLOGICAL PRODUCTS: **BIOTECHNOLOGICAL PRODUCTS S.D. Nº 011-2016-SA**

- Biotechnological products are those biological products obtained by biotechnological procedures, such as:
  - DNA Recombinant techniques
  - Monoclonal antibody and hybridome techniques
  - Other methods determinate by the ANM in accordance to the advance of science

Source: http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_011-2016.pdf

SUPREME DECREE Nº 011-2016-SA
February 27th, 2016

- Quality requirements should be accompanied by a resume that includes information of all quality aspects emphasizing critical parameters, with an analysis that integrates quality data and preclinical and clinical data.

- This document became effective on Aug 25, 2016

Source: http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_011-2016.pdf

SPECIFIC REGULATIONS:

REGULATION ABOUT THE SUBMISSION AND CONTENT OF THE DOCUMENTS REQUIRED FOR THE SANITARY REGISTRATION AND RE-REGISTRATION OF BIOLOGICAL PRODUCTS: BIOLOGICAL PRODUCTS THAT CHOOSE THE SIMILARITY PATHWAY.
S.D. Nº 013-2016-SA

- Includes terms of comparability exercise, reference biological product, similar biological product.
- Biological products that could chose the similarity pathway are those whose APIs are well characterized.

Source: http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_013-2016.pdf

SUPREME DECREE Nº 013-2016-SA
March 1st, 2016

- The quality module according to CTD should include complete data, additionally, should present the comparability exercise between SBP and RBP in terms of quality.
- Reduction data requirements is possible for pre-clinical and clinical aspects.
- It includes criteria for the justification of selection of a RBP and the information that allow set up comparability from the point of view of quality, safety and efficacy.
- This document became effective on Aug 28, 2016

Source: http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_013-2016.pdf

ABOUT THE NEW SPECIFIC REGULATIONS

- Give more specific requirements for biotechnological and similar biological products.
- Introduce terms of Common Technical Data, immunogenecity, intermediates, reprocessing and impurities.
- The documentation should comply with the recommendations of: WHO, PANDRH, ICH, EMA, Health Canada, and/or FDA.
- Both regulations consider a stepwise approach to update the technical documentation of approved products.

Source:
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_011-2016.pdf
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_013-2016.pdf1

ABOUT THE NEW SPECIFIC REGULATIONS

❑ Content of documents to apply for registration or re-registration:

- General Information
- Technical Information

Application form (Affidavit). 1

- Specifications and justifications
- Techniques and validations
- Batch Analysis
- Characterization of impurities

Quality control documentation of API, finished product and excipients 2

- API and finished products
- Specifications

Standards and reference material 3

- API and finished products
- Description and flow chart of manufacturing process.
- Control in Process, critical stages and intermediates

Manufacturing process description and its validation 4

- API and finished product stability studies.

Stability studies 5

Source:
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_011-2016.pdf
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_013-2016.pdf

ABOUT THE NEW SPECIFIC REGULATIONS

- Content of documents to apply for registration or re-registration:

Certificate of Pharmaceutical Product 6
- Or Free Sale Certificate issued by the competent authority of origin country

Good Manufacture Practices Certificate 7
- Of national or overseer manufacturer.
- Issued by DIGEMID, high surveillance countries and those which have mutual recognition with PERU.

Container closure system 8
- API and finished product
- Description of the components of the container closure system and technical specifications

Characterization and pharmaceutical development 9
- API Characterization: Determination of structure and other characteristics, impurities
- Pharmaceutical development of finished product, components, formulation development.

Technical sheet and package insert 10
- According to the content of this Regulations.

Source:
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_011-2016.pdf
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_013-2016.pdf

ABOUT THE NEW SPECIFIC REGULATIONS

- Content of documents to apply for registration or re-registration:

Project of labeling of mediate and immediate packages 11
- According to the content of this Regulations and the information requested in the pharmacopoeia reference

Pre clinical studies 12
- When applies

Clinical studies 13
- Present the clinical studies phase 1, 2 and 3

Risk planning management 14
- According to the established in the regulation

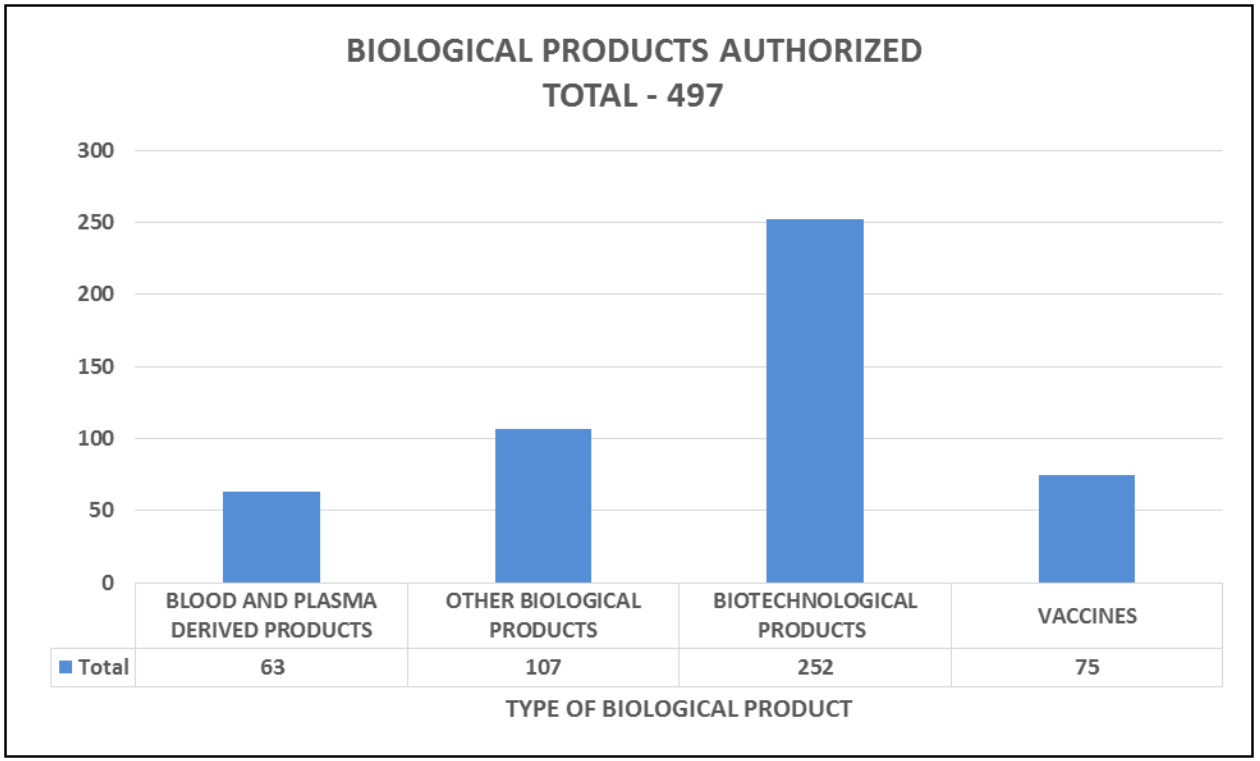
Source:
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_011-2016.pdf
http://www.digemid.minsa.gob.pe/UpLoad/UpLoaded/PDF/Normatividad/2016/DS_013-2016.pdf

SPECIFIC REGULATIONS:IN PROJECT

PROJECT OF THE REGULATION FOR THE EXPEDITION OF BATCH RELEASE CERTIFICATED OF BIOLOGICAL PRODUCTS: VACCINES OR PLASMA DERIVED PRODUCTS

- Published In April 6, 2017, it is in the phase of receiving suggestions and comments during a period of 90 calendar days.
- Establishes the rules to be followed and the documents required prior to the request for issuance of the batch release certificate.
- The application is submitted for each lot and for each entry to the country of the same lot.

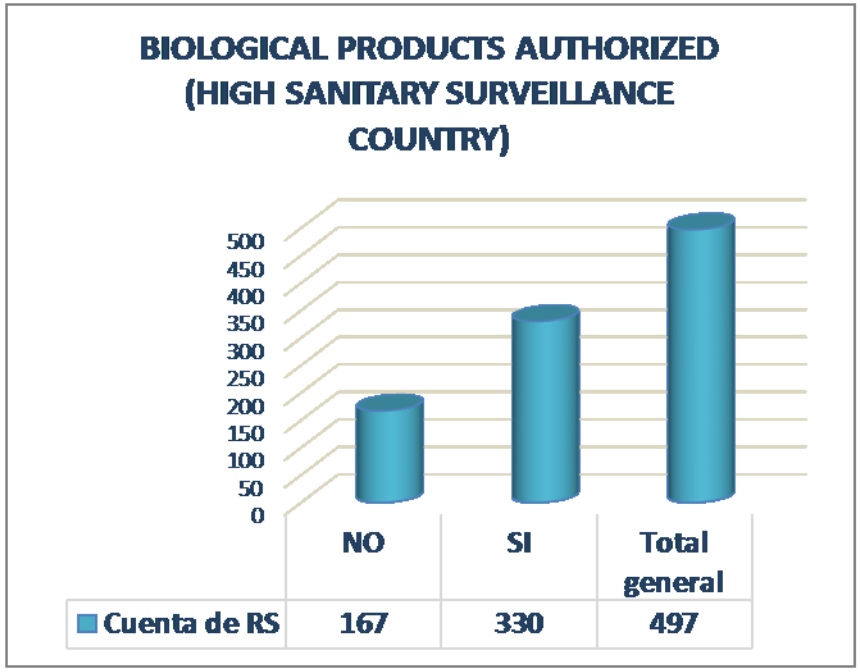
BIOLOGICAL PRODUCTS AUTHORIZED



- Since January 8th, 2016 new requirements for biological products are in force based on S.D. 016-2011 and amendments.
- DIGEMID has regulation for products obtained by biotechnological process and is working in developing regulation for the other groups.

Source: Data of ATIC-DIGEMID May 2017

BIOLOGICAL PRODUCTS AUTHORIZED



- Authorities of countries of high surveillance (PAV) are: France, Holland, United Kingdom, United States, Canada, Japan, Switzerland, Germany, Spain, Australia, Denmark, Italy, Norway, Belgium, Sweden, Republic of Korea, Portugal, EMA

Source: Data of ATIC-DIGEMID until Mary 2017

SOME CHANGES IN REVIEW PROCESS

- DIGEMID have developed new specific regulations for registration and re-registration of vaccines, blood and plasma derived products and other biological products, requirements for modifications in the sanitary registration and stability studies for biological products. which are in review phase.
- Since 2012, DIGEMID conforms a team in charge of the review of biological products.
- Currently the group have 10 technical evaluators.

Currently

- The group of biological products is receiving national and international training.
- DIGEMID is preparing to get the qualification as a reference authority for medicines and biologicals of the Pan American Health Organization.
- Management Quality System of DIGEMID has been recertified by ICONTEC in ISO 9001:2008

Pan American Health Organization

ISO 9001 icontec

A view to the future

- Approval of regulations for biological products (vaccines , plasma and blood derived products, stability, batch release).
- Develop regulations for other biological products.
- Apply good review practices, procedures and templates in the review process.

International Perspectives

- Share experiences with other countries, that have similar challenges; also, learn of other NRA with more experience in the world and in our region, and contribute with our experience building new regulations.
- Participate in international training, workshops and virtual meetings with harmonization approach.

Thank you…

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