AN OVERVIEW OF THE REGULATION OF BIOTECHNOLOGICAL AND BIOSIMILAR PRODUCTS IN PERU

Ana Maria Agueda Chura Tito
Area of Biological Products- UFPBNDYO
Directorate of Pharmaceutical Products
General Directorate of Medicines, Supplies and Drugs (DIGEMID)
Ministry of Health (MINSA) - Peru
OUTLINE

• Introduction of DIGEMID
• Legal Bases of Biological Products in Peru
• Regulation of biotechnological and biosimilar products
• Conclusions
GENERAL DIRECTORATE OF MEDICINES, SUPPLIES AND DRUGS

PHARMACEUTICALS PRODUCTS DIRECTORATE

MEDICAL DEVICES AND SANITARY PRODUCTS DIRECTORATE

INSPECTION AND CERTIFICATION DIRECTORATE

PHARMACOVIGILANCE, ACCESS AND USE DIRECTORATE

FUNCTIONAL UNIT OF MEDICINES

FUNCTIONAL UNIT OF BIOLOGICAL PRODUCTS, NATURAL, DIETETIC AND OTHERS

FUNCTIONAL UNIT OF CONTROLLED PRODUCTS

Source: http://www.digemid.minsa.gob.pe/
GENERAL DIRECTORATE OF MEDICINES, SUPPLIES AND DRUGS

- Created in April 18, 1990, as a line organ of the Ministry of Health.
- Located in Lima, Perú.
- Total staff: About 600 (10 in biological review).
- The main objective is to ensure access and rationally use to safe, effective and quality medicines.

Source: [http://www.digemid.minsa.gob.pe/](http://www.digemid.minsa.gob.pe/)
LEGAL BASES OF BIOLOGICAL PRODUCTS

Law 29459
Law of Pharmaceutical, Medical Devices and Health Products (Nov 26th, 2009)

Supreme Decree 016-2011 and amendments
Registration, Control and Health Surveillance of Pharmaceutical Products, Medical Devices and Health Products (Jan 23th, 2011)

Supreme Decree N° 011-2016-SA
Registration and re-registration of biotechnological products (Feb 27th, 2016)

Supreme Decree N° 013-2016-SA
Registration and re-registration of biological products that choose the similarity pathway (Mar 1st, 2016)

Defines basic principles of safety, efficacy and quality.

Definition, classification and general requirements for registration and re-registration

Submission and content of the documents required for the sanitary registration and re-registration

Source: http://www.digemid.minsa.gob.pe
Supreme Decree 016-2011-SA and Amendments
Chapter V. Biological Products

- Define specific aspects of Law N° 29459.
- Describe general requirements for biological products: full data of quality, efficacy and safety.
- Establish classification for biological products.
- Describe general requirements to submit and evaluate similar biological product: based in WHO’s recommendations.
- Since January 8th, 2016 new requirements for biological products are in force based on S.D. 016-2011 and amendments.

Supreme Decree 016-2011-SA and Amendments
Chapter V. Biological Products

- **Classification for Biological Products (Article 103°):**

  - **Biological Products**
    - **Immunological**
      - Vaccines
      - Allergens
      - Serums
    - **Blood and plasma derived products**
    - **Biotechnological Products**
      - DNA Recombinant techniques
      - Monoclonal antibody and hybridoma techniques
      - Other methods determinate by DIGEMID in accordance with the advance of science
    - **Other biological products.**

Requirements for marketing authorization of Biological Products

- Application form (Affidavit)
- Project of labelling, Technical sheet and package insert
- Certificate of Pharmaceutical Product
- Good Manufacture Practice Certificate (GMP)
- Certificate of batch release
- Risk Management Plan
- Summarize the quality, pre-clinical, and clinical information presented in modules 3, 4, and 5 in the market authorization application
- Quality control documentation of API, finished product and excipients.
- Standards and reference material of API and finished product
- Manufacturing process description of API, finished product and its validation.
- Stability studies
- Container closure system
- Characterization of API and pharmaceutical development of finished product.
- Certificates of suitability for TSE compliance
- Negative certificate of HIV, hepatitis B and C

The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region-specific and modules 2, 3, 4, and 5 are intended to be common for all regions.
REFERENCE PHARMACOPEIA

- United States Pharmacopeia (USP)
- British Pharmacopeia (BP)
- European Pharmacopoeia (Ph. Eur.)
- Japanese Pharmacopoeia
- International Pharmacopoeia (Ph.Int.)
- German Pharmacopoeia
- Pharmacopoea Helvetica (Ph. Helv.)
- Belgian Pharmacopoeia
- Korean Pharmacopoeia

AUTHORITIES OF HIGH SANITARY SURVEILLANCE COUNTRIES

France, Holland, United Kingdom, United States of America, Canada, Japan, Switzerland, Germany, Spain, Australia, Denmark, Italy, Norway, Belgium, Sweden, Republic of Korea, Portugal and Ireland

Fuente: http://bvcenadim.digemid.minsa.gob.pe/enlaces/agencias-reguladoras-de-paises-de-alta-vigilancia-sanitaria
Supreme Decree 016-2011-SA and Amendments
Chapter V. Biological Products

- To establish specific requirements for biological products.

- Complete information of quality, efficacy and safety.

- Two ways to apply for marketing authorization:
  - Biological product with full data of quality, safety and efficacy.
  - Biological product that claimed to be similar to Reference Biological Product (RBP)

- Evaluation time: vaccines and immunological products shall not exceed one hundred and eighty (180) calendar days. The period for the rest of biological products is up to twelve (12) months.

Fuente: Data del SI-DIGEMID/PB hasta octubre del 2016
LEGAL BASES OF BIOLOGICAL PRODUCTS

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Source: http://www.digemid.minsa.gob.pe
Regulation of biotechnology products and biological products which choose the way of similarity

Supreme Decree
Nº 011-2016-SA
February 27th, 2016

Document that regulates the presentation and content of the requirements for marketing authorization of Biotechnological Products

COMING INTO FORCE
(August 25th, 2016)

Supreme Decree
Nº 013-2016-SA
March 1st, 2016

Document that regulates the presentation and content of the requirements for marketing authorization of Biological Products which choose the way of similarity

COMING INTO FORCE
(August 28th, 2016)
ENTRADA EN VIGENCIA DEL REGLAMENTO 60-calendario-day

NOTIFY TO THE DIGEMID THEY NOT CHOOSE THE WAY OF SIMILARITY

60-calendario-day

PRODUCTS WITH SANITARY REGISTRATION IN FORCE

COMING INTO FORCE OF REGULATIONS (August 25th, 2016)

NOTIFY TO THE DIGEMID THEY NOT CHOOSE THE WAY OF SIMILARITY

Risk Management Plan

PRODUCTS IN REGISTRATION PROCESS: IS COUNTED FROM OBTAINING SANITARY REGISTRATION

6 MONTHS

1 YEAR

UPDATE DOCUMENTATION ON MARKETING AUTHORIZATION IN FORCE

QUALITY CONTROL, STANDARDS, MANUFACTURING AND ITS VALIDATION, STABILITY, CONTAINER CLOSURE SYSTEM, CHARACTERIZATION, PHARMACEUTICAL DEVELOPMENT, PRE-CLINICAL STUDIES, CLINICAL STUDIES

BIOTECHNOLOGICAL PRODUCTS WHICH NOT CHOOSE THE WAY OF SIMILARITY (D.S.N 011-2016-SA)
ENTRY INTO VIGOR OF THE REGULATIONS

- PRODUCTS WITH SANITARY REGISTRATION IN FORCE
- COMING INTO FORCE OF REGULATIONS (August 28th, 2016)

- NOTIFY TO THE DIGEMID WHETHER THEY WILL OPT TO DEMONSTRATE BIOSIMILARITY

- Risk Management Plan

- QUALITY CONTROL, STANDARDS, MANUFACTURING AND ITS VALIDATION, STABILITY (EXCEPT COMPARABILITY), CONTAINER CLOSURE SYSTEM, CHARACTERIZATION (EXCEPT COMPARABILITY), PHARMACEUTICAL DEVELOPMENT

- PRE-CLINICAL STUDIES, ESTABILITY (COMPARABILITY) CHARACTERIZATION (COMPARABILIT)

- CLINICAL STUDIES

- PRODUCTS IN REGISTRATION PROCESS: IS COUNTED FROM OBTAINING SANITARY REGISTRATION

- 60 - calendar day

- 6 MONTHS

- 18 MONTHS

- 3 YEARS

- 5 YEARS

UPDATE DOCUMENTATION ON MARKETING AUTHORIZATION IN FORCE

BIOLOGICAL PRODUCTS WHICH CHOOSE THE WAY OF SIMILARITY (D.S.N 013-2016-SA)
REGULATION OF BIOTECHNOLOGICAL AND BIOSIMILAR PRODUCTS

- Give more specific requirements for biotechnological and similar biological products, and complement general requirements covered in Supreme Decree N° 016-2011-SA.
- The documentation should be presented according to CTD, and should comply with the recommendations of: WHO, PANDRH, ICH, EMA, Health Canada, and/or FDA.
- Quality requirements should be accompanied by a resume including information of all quality aspects emphasizing critical parameters, with an analysis that integrates quality data and preclinical and clinical data.
- In the case of biological products that choose the way of similarity, the quality module 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.
- Both regulations consider a stepwise approach to update the technical documentation of approved products.

Source: [http://www.digemid.minsa.gob.pe](http://www.digemid.minsa.gob.pe)
Some changes in review process

- New regulations introduce changes in our regulation and therefore, evaluators and the industry need adaptation of the changes as well.
- Since 2012, DIGEMID conforms a team in charge of the review of biological products.
- Currently the group have 10 technical evaluators.
- The Team of biological products is developing new specific regulations for vaccines, blood and plasma derived products, and other biological products.
# BIOLOGICAL PRODUCTS AUTHORIZED

<table>
<thead>
<tr>
<th>Biological Product</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and plasma derived products</td>
<td>67</td>
</tr>
<tr>
<td>Immunological-serum</td>
<td>1</td>
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<tr>
<td>Immunological-vaccine</td>
<td>73</td>
</tr>
<tr>
<td>Other biological</td>
<td>92</td>
</tr>
<tr>
<td>Biotechnological Products - DNA Recombinant techniques</td>
<td>186</td>
</tr>
<tr>
<td>Biotechnological Products - Monoclonal antibody and hybridoma techniques</td>
<td>45</td>
</tr>
</tbody>
</table>

Fuente: Data SI-DIGEMID/PB. ATIC, April 12th, 2018
CONCLUSIONS

- New regulations introduce a substantial change in the regulations of Digemid.
- There are more new specific regulations to be issued: post approval changes, stability studies, vaccines, blood plasma derived products, batch release, and other biological products.
- DIGEMID is preparing to get the qualification as a reference authority for medicines and biologicals of the PAHO.
- Technicals participate in international training, workshops and virtual meetings sharing experiences with other countries and learning from other NRA with more experience.
Inquires/Questions: http://www.digemid.minsa.gob.pe
achura@digemid.minsa.gob.pe