An Overview of National Regulatory Requirements for Biological Products in Peru

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Outline

• Description biological products in Peru
• Legal and technical development
• Biological product distribution
• Biological product safety
• Clinical trials with biological products
• Conclusions
General

- Estimated population to 2014: 30 814 175 millions of people
- Life expectancy to 2014: 74.4 years
- GDP per capita to 2012: 17 852.69 “New Soles” per person
- Health coverage to 2012: 61.9%
- Biological Products represent 4% (514/11 625) of all the pharmaceuticals and related products with sanitary registration in force.

Source: http://www.inei.gob.pe/
Biological Products manufactured

- Botropic polyvalent serum
- Antilachesico monovalent serum
- Antiloxoscelico monovalent serum
- Biolactol probiotic acidophilus
- Vaccine Gel NB probiotic
- Enoxaparin
- Heparin sodium

Nowadays, 514 biological products authorized (with sanitary registration), of which 8 are locally manufactured.

Source: Data of SIS-DIGEMID
Legal and technical development of biological products in Peru

Political Constitution
Article 118°, subsection 8

Legal Development

Law 26842, in 1997
General Health Law

Law 29459, in 2009
Law of Pharmaceuticals, Medical Devices and Health Products

Technical Development

D.S. 010-1997
Registry Regulations, Health Surveillance and Control of Pharmaceutical and related Products
Includes regulations for biological products

D.S. 016-2011 and amendments
Regulation for Registration, Control and Health Surveillance of Pharmaceutical Products, Medical Devices and Health Products
Chapter V: biological products

Source: http://www.digemid.minsa.gob.pe/Main.asp?Seccion=727
Regulatory change based on the Law of Pharmaceuticals, Medical Devices and Health Products

<table>
<thead>
<tr>
<th>D.S. 010-1997</th>
<th>D.S. 016-2011</th>
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<tbody>
<tr>
<td>- No differences between the requirements for registering chemical products and biological products</td>
<td>- To Establish specific requirements for biological products</td>
</tr>
<tr>
<td>- Evaluation time: 7 days</td>
<td>- Evaluation time: vaccines and immunological products, up to 180 days. Other biological products, the period is 12 months</td>
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D.S. 016-2011. In force
About of definitions of biological product

• In Peru, Biological and Biotechnological products are considered under the same concept: BIOLOGICAL PRODUCT

• Follows the definition of World Health Organization

D.S. 016-2011. In force
Chapter V: biological products

- According to the principles of quality, efficacy and safety
- Has 12 articles
- To establish requirements for registration and re-registration
- To designate the term “Similar biological product” (article 107°)
- Two pathways of register a biological product: complete dossier or similarity way

D.S. 016-2011- Chapter V: biological products

Article 102°: Sanitary registration of biological products

Article 103°: In biological products

Article 104°: Requirements for registration and re-registration of biological products

Article 105°: Application contents - affidavit of registration or re-registration of biological products

Article 106°: Requirements for granting a certificate of batch release

Article 107°: Similar biological product

D.S. 016-2011- Chapter V: biological products

Article 108°: Time limits for sanitary registration of biological products

Article 109°: Labeling of mediate and immediate packaging of biological products

Article 110°: Information contained in the data sheet and insert biological products

Article 111°: Condition of sale of biological products

Article 112°: In the periodic reports of safety of biological products

Article 113°: Coding of sanitary registration of biological products

Assessment process

• Peru follows and/or considers internationally accepted standards like those of the WHO, FDA, and EMA guidelines.

• Article 107°: Similar Biological Product ... “Specific aspects of the quality requirements, preclinical and clinical studies of biological products who choose the way of similarity will be identified in individual directives, taking into account the progress of science and the recommendations of the WHO.”

• Has been working on the proposal of the Technical Documents for:
  
  - Similar biological products
  - Biotechnological products (full dossier)

• In the next years:
  
  - Technical document for vaccines
  - Technical document for plasma derived
Technical Document for Similar biological products. Draft

• Recommendations for the Evaluation of Similar Biotherapeutics Products of PARF network/WHO; as well as some specific guidelines issued by ICH, FDA, EMA and Health Canada.

• Definitions: similar biological product (SBP), reference biological product (RBP) and comparability exercise.

• SBP and RBP:
  - Full characterization and comparison in terms of quality are the basis for possible data reduction in pre-clinical and clinical development.
  - Case by case analysis approach

• Transitional provisions
Biological products authorized

- Has been authorized as biological products since 1998

- N total = 514 biological products with sanitary registration

- 77% (398) with sanitary registration in force

- 23% (116) in re-registration process

Source: Data of SIS-DIGEMID
Biological products authorized by kind of biological products

Source: Data of SIS-DIGEMID

N total = 514 biological products with sanitary registration
Biological products authorized from High Sanitary Surveillance Countries (HSSC)

According to article 9° of D.S. 016 - 2011

N total = 514 biological products with sanitary registration
Distribution of biological product authorized

Overall, in Peru we can identify two channels of drug distribution:

- Public Health Sector: MINSA, Regional Governments and EsSalud

- Private Health Sector
Consumption of biological products in EsSalud: 2012 and 2013

Source: Data of Access to Drugs Team of the Directorate of Access and Use of Drugs
Consumption of biological products in MINSA and Regional Governments: 2012 and 2013

Source: Data of Access to Drugs Team of the Directorate of Access and Use of Drugs
Biological Product Safety

• n = 265 biological products with sanitary registration

• Spontaneous reporting

• 31% (82/265) of biological products reported any adverse reactions

• 19% (49/265) of biological products reported serious adverse reactions

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<thead>
<tr>
<th>Biological Product</th>
<th>Number of Biological Products</th>
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<tbody>
<tr>
<td>Vaccines</td>
<td>12</td>
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<tr>
<td>Monoclonal antibody</td>
<td>7</td>
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<tr>
<td>Enzimas</td>
<td>5</td>
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<tr>
<td>Hormones</td>
<td>5</td>
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<tr>
<td>Heparins</td>
<td>4</td>
</tr>
<tr>
<td>Insulins</td>
<td>3</td>
</tr>
<tr>
<td>Interferons</td>
<td>3</td>
</tr>
<tr>
<td>Erythropoietin / epoetin</td>
<td>2</td>
</tr>
<tr>
<td>Coagulation factors</td>
<td>2</td>
</tr>
<tr>
<td>Immunoglobulins</td>
<td>2</td>
</tr>
<tr>
<td>Colony Stimulating Factor</td>
<td>1</td>
</tr>
<tr>
<td>Plasma substitute</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>49</td>
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Source: Data of Pharmacovigilance Team of the Directorate of Access and Use of Drugs
Clinical trials authorized with biological products: 2012 and 2013

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<th></th>
<th>2012</th>
<th>2013</th>
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<tr>
<td>Total applications for clinical trials (chemical and biological products)</td>
<td>130</td>
<td>92</td>
</tr>
<tr>
<td>Authorized clinical trials with biologicals</td>
<td>37</td>
<td>29</td>
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</tbody>
</table>

Source: Data of General Office of Research and Technology Transfer - National Institute of Health
Clinical Trials authorized with biological products by phases of the study: 2012 and 2013

Source: Data of General Office of Research and Technology Transfer - National Institute of Health
Clinical Trials authorized with biological products by medical specialty

Source: Data of General Office of Research and Technology Transfer - National Institute of Health
Conclusions

• In Peru, approval of biological products is given in accordance with the requirements of DIGEMID, based on “Law of Pharmaceuticals, Medical Devices and Health Products”

• Nowadays, 98% of biological products with sanitary registration are imported.

• Biological and Biotechnological products are considered under the same concept: BIOLOGICAL PRODUCT
Conclusions

• The trend in Peru is toward the adoption of accepted international standards, like those presented by the WHO.

• DIGEMID is committed to ensuring the quality, efficacy and safety of biological products.
Acknowledgements

• General Office of Research and Technology Transfer - National Institute of Health.
• Pharmacovigilance Team of the Directorate of Access and Use of Drugs.
• Access to Drugs Team of the Directorate of Access and Use of Drugs.
• Efficacy and Security Area of Directorate of Sanitary Authorizations.
Thank you