FEDERAL COMMISSION FOR THE PROTECTION FROM SANITARY RISKS

Sanitary Authorisation Commission

Regulatory Framework for the Biotherapeutic Products in Mexico
Overview

- Definitions and Legal Framework
- Biotechnological product vs Biosimilar
- Regulatory process of biotechnological and biosimilar marketing authorisation
- New Molecules Committee and Subcommittee of Biotecnological Products
- Current situation
Definitions

- Biotechnological product: each product that has been produced by molecular biotechnology.

- Biosimilar product, each biotechnological product that prove biocomparability in terms of safety, efficacy and quality, between the reference product.

- Reference product is the biotechnological product recognized by Mexican Health Ministry, and they can be used for the biocomparability exercises.
Legal Framework

- Political Constitution
- General Health Law
- Regulation for Health products
- Official Mexican Standards
- Others
Legal Framework Transition

- 2009
  General Health Law

- 2011
  Regulation HP

- 2012
  NOM-EM-001-SSA1-2012

- 2013
  NOM-177-SSA1-2013

- 2014
  NOM-257-SSA1-2014
Biotechnological product vs Biosimilar

Biosimilar

SAME

Biocomparable
Biotechnological product vs Biosimilar

Comparability Exercise: Head-to-head comparison in terms of quality, safety and efficacy.

REFERENCE PRODUCT

BIOSIMILAR

Quality information

Pre-clinical Studies

Clinical Studies

Extensive

Reduced

Full characterization is the basis for the possible reduction of clinical data.

Reduced
## Biotechnological product vs Biosimilar

<table>
<thead>
<tr>
<th>Type of product</th>
<th>Information to be submitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotechnological</td>
<td>Module I: Administrative and Legal&lt;br&gt;Module II: Quality Information&lt;br&gt;Module III: Preclinical studies&lt;br&gt;Module IV: Clinical studies</td>
</tr>
<tr>
<td>Biosimilar</td>
<td>Module I: Administrative and Legal&lt;br&gt;Module II: Quality Information&lt;br&gt;Module III: Biosimilar studies (more characterization less clinical trials)</td>
</tr>
</tbody>
</table>
Process for Biotechnological and Biosimilar products approval

**Pre-Marketing**
- Submission Dossier For MA
  - Protocol approval
  - Clinical Trials
    - NMC and BPSE approval
  - Studies of biocomparability
    - Third Authorized parties

**Evaluation Process of Medicines**
- Group of experts in COFEPRIS, they only evaluate biotech

**Post-Marketing**
- Advertising
- Marketing

**Pharmacovigilance**
- GMP’s
Evaluation process. Biotechnological products

All the information is pre review for the New Molecules Committee

**CLINICAL TRIALS**

**MANUFACTURING**

- Regulation
- Approval
- Surveillance

PRE CLINICAL AND CLINICAL INFORMATION
(Takes place in Mexico or others countries)

*Drug Substance: e.g., General Information, characterization, control of drug substances, reference standards, etc.*

*Drug Product: e.g., Description and composition of the drug product, pharmaceutical development, manufacture, control of excipients, control of drug product, stability, etc.*
New Molecules Committee and Subcommittee of Biotechnological Products

The NMC and SBP are instances of consultation, the Committee and Subcommittee evaluate the information about safety, efficacy and quality of the new medicines or new indications for the purpose of registration, or products which require to be evaluated by groups of specialists.

The permanent members are: Sanitary Authorisation Commissioner, Director of Marketing Authorisation, National Center of Pharmacovigilance, the Analytical Control and Coverage Extension Commission, the Mexican Institute of Industrial Property, Health institutes, Mexican Institute of Social Security (IMSS), the National Academy of Medicine, among others.

The NMC and SBP have 2 meetings per week, so it is possible to review 1 product each meeting.

The technical opinion of the NMC is described in an official document. This document is sent to the manufacturer.
The Subcommittee of Biotechnological Products was created regarding the modification of the General Health Law.

The Subcommittee is constituted for external expert in the next topics:

- Biotechnology
- Manufacture
- Immunology
- Pharmacovigilance
- Genetic
- Etc…
Process of Subcommittee of Biotechnological Product

Sponsor

COFEPRIS

Send information to Experts of the SBP

COFEPRIS

Subcommittee experts

Evaluate Information

Biosimilarity studies to carry on in Mexico

Or

Information is enough

Meeting with the NMC

Official opinion

Sponsor

Carry on biosimilarity studies

Or

MA process

Biosimilarity information (if exists)
Assessment process

- Development product
- Biosimilars
- Final product
- New therapeutic Indication
- Final product
- First time meeting
- Following meeting
- First time meeting
- Following meeting
- Equivalence agreement
- Traditional process
Evaluation of new biotechnological products, innovator or biosimilar, in process of research and development. Following up process.

Evaluation of new biotechnological products, innovator or biosimilar.

Defined the reference products according to the official standards.
Information that have to be review for the New Molecules Committee

- Clinical Trials
- SBP opinion
- Risk Management Plan
- Patent (Industrial property)
Information that have to be review for the Subcommittee of Biotechnological Products
### SOLICITUD DE REUNIÓN ANTE EL SUBCOMITÉ DE EVALUACIÓN DE PRODUCTOS BIOTECNOLÓGICOS

<table>
<thead>
<tr>
<th>Razón Social</th>
<th>No. Trámite</th>
<th>Fecha Ingreso solicitud</th>
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<tr>
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<table>
<thead>
<tr>
<th>Nombre del Propietario o Representante Legal</th>
<th>RFC</th>
<th>CURP</th>
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<tbody>
<tr>
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<tr>
<td>Localidad</td>
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<td>(Lada)Teléfono</td>
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<table>
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<tr>
<th>Tipo de reunión</th>
<th>Tipo de producto</th>
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</thead>
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<tr>
<td>ORDINARIA</td>
<td>Producto terminado (2)</td>
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<tr>
<td>SEGUIMIENTO (1)</td>
<td>Producto en desarrollo (3)</td>
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<tr>
<td>EXTRAORDINARIA</td>
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(1) En caso de que se haya presentado anteriormente indicar:
(3) Indicar la etapa de evaluación:

<table>
<thead>
<tr>
<th>Tipo de solicitud</th>
<th>(2) Tipo de solicitud</th>
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</thead>
<tbody>
<tr>
<td>Nuevo registro</td>
<td>Modificación (4) (5)</td>
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<tr>
<td>Prorroga (4)</td>
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</tbody>
</table>

(4) No. Reg. Sanitario: 
(5) Indicar la modificación solicitada:

En caso de tratarse de un nuevo registro, prorroga, modificación a principio de este cuadro, relacionado con la reunión indicar:

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<thead>
<tr>
<th>No. de trámite</th>
<th>Fecha de Ingreso</th>
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Mexican Official Standards of Biotechnological Products

2013

NOM-177-SSA1-2013

- Requirements for authorized 3rd parties to perform biocomparability exercises.

2014

NOM-257-SSA1-2014

- Biotechnological products.
Mexican Official Standards

NOM-177

General requirements

Equipment and Facilities

Reference product

Quality Management System

Comparability exercises

Human resources
Manufacturing controls of biotechnological product

- Quality assurance program
  - Validation program
  - Critical parameters
  - Audit/Inspection program for process and product
  - Corrective and preventive actions program

Annual report

Requirement for renovation (innovator and biosimilars)
COFEPRIS has made equivalence agreements for drug approval, which allow that registered drugs in other countries could be approved expeditiously in Mexico.

The agreements are published in the web page of COFEPRIS (www.cofepris.gob.mx)
Current Situation

Guideline publication of minimal biocomparability requirements for: insulin, filgrastim, somatropine, interferon, infliximab, and etanercept

- Physical-chemical and biological characterization
- Preclinical studies
- Clinical trials

This guidelines was generated to help the MA holders, and to clarify the requirements.

However, the evaluation of each biotechnological or biosimilar product is case by case.
Current Situation

- Publication list of 67 biotechnology reference products, which can be found at the following web site: http://www.cofepris.gob.mx/AS/Paginas/Registros%20Sanitarios/RegistroSanitarioMedicamentos.aspx
Current Situation

- We have officially recognized 4 biosimilar products: Sandoz, Celltrion, Eli Lilly and National Manufacturer (PISA).

- Recognition of 4 third party centers to conduct biocomparability studies.
Third authorized parties

HEALTH CONTROL
COFEPRIS

- Laboratory testing
- Units for Bioequivalence and biocomparability studies
- Units for GMP inspections
- Units for pre-review of drugs and medical devices dossiers

QUALITY SYSTEM ISO 17025
NOM 177
QUALITY SYSTEM ISO 17020
Current Situation

• We are participating at this prestigious APEC conference. The intention is to work in cohesive manner to harmonized our guidelines, criteria and documents.

• Additionally, we will participated in the IPRF meetings.

• Requirements of extrapolation and modifications.
Conclusions

- Quality, safety and efficacy
- Access to drugs
- Harmonization
MUCHAS GRACIAS

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ahernandezt@cofepris.gob.mx

We are COFEPRIS,
we are NRA