Regulatory considerations for biological products in Brazil

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Brazilian Health Surveillance Agency – ANVISA

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Anvisa’s Overview

Anvisa’s Mission

To protect and promote the public health and to intervene in the risks caused by the production and use of products subject to health surveillance, in coordination with the states, municipalities and the Federal District, according to the Brazilian Health System principles, in order to improve the quality of life of the population.
Anvisa’s Overview
Areas of action

- Food
- Cosmetics
- Sanitizing Products
- Tobacco
- Toxicology (pesticides)

- Health services
- Drugs
- Medical Devices
- Laboratories
- Blood, Cells, Tissues and Organs

- Post-marketing surveillance
- Marketing control
- Ports, airports and frontiers
- International
- Market regulation
Anvisa’s Overview
Organization chart

General Office of Biologicals
Regulatory Acts Concerning Biological Products

- Labeling
  - RDC 47/2009
  - RDC 60/2012
- Package insert
  - RDC 71/2009
  - RDC 61/2012
- Import
  - RDC 81/2008
- Quality control
  - RDC 234/2005
- Good manufacturing practices
  - RDC 17/2010
- Blood products
  - RDC 46/2000
- Allergenics
  - RDC 233/2005
- Probiotics
  - RDC 323/2003
- Stability
  - RDC 50/2011
  - RDC 25/2013
- Antivenom serums
  - Ordinance 174/1996

- Law 6.360/1976
- Decree 8.077/2013
- Marketing Authorization
  - RDC 55/2010
- Post-approval changes
  - RDC 49/2011
  - RDC 24/2013
I. Vaccines

II. Antivenom immunoglobulins

III. Blood products

IV. Biomedicines, obtained from:
   a) Biological fluids or animal tissues
   b) Biotechnological procedures

V. Monoclonal antibodies

VI. Medicines containing live, attenuated or dead microorganisms

VII. Probiotics

VIII. Allergens
Biological Products
Current Regulation

RDC 55/2010

I - New Biological Product

Is the biological medicine containing a molecule with a known biological activity, still not licensed in Brazil, and that has undergone all stages of manufacturing → innovative product.

II - Biological Product

Is the biological medicine that is not new or is already known, containing a molecule with a known biological activity, already licensed in Brazil, and that has undergone all stages of manufacturing → non-innovative product.
Biological Products
Current Regulation

New Biological Product
  Complete Dossier
    Quality, Safety and Efficacy

Biological Product
  Stand Alone Pathway
    Complete Dossier
      Comparative Clinical Trials

  Comparability Development Pathway
    Complete Dossier
      Comparability Exercise
        Quality, Safety, Efficacy

STAND ALONE

BIOSIMILARS
Brazilian regulation for biological and biosimilar products is aligned with WHO recommendations;

Regardless of the regulatory pathway chosen to license a biological product in Brazil, RDC 55/2010 demands proof of quality, safety and efficacy of all products.
<table>
<thead>
<tr>
<th>EMA</th>
<th>FDA</th>
<th>Health Canada</th>
<th>Anvisa</th>
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<tbody>
<tr>
<td>Individual countries in EU have adopted varying policies</td>
<td>US law allows FDA to designate a product as interchangeable. However, decisions about substitution by the pharmacy are governed by state laws</td>
<td>Health Canada doesn’t declare interchangeability for biosimilars</td>
<td>Interchangeability is under discussion. Currently, Anvisa only considers interchangeability after the review of the clinical data obtained for this purpose</td>
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Extrapolation of therapeutic indications

Reflection paper on extrapolation of indication

- Discussion group about the theme to propose a reflection paper.

- Strong scientific justification for extrapolation of indication by companies should be emphasized in the paper.
International non-proprietary name or INN

WorId Health Organization

INN Working Doc. 14.342
Revised draft June 2015
Distr.: RESTRICTED
ENGLISH ONLY

Biological Qualifier
An INN Proposal

Programme on International Nonproprietary Names (INN)

Technologies Standards and Norms (TSN)
Regulation of Medicines and other Health Technologies (RHT)
Essential Medicines and Health Products (EMP)
World Health Organization, Geneva
Board of Directors Resolution – RDC nº 63/2012

Provides the rules used for the Brazilian Non-proprietary Names - DCB.
Top 3 Challenges

1. Interchangeability
2. Extrapolation of indications
3. International non-proprietary name or INN
Biological Products
Current Regulation

- Product life cycle
- RDCs 49/11, 25/13
- RDCs 50/11, 25/13
- RDC 55/10

Marketing Authorization
RDC 49/2011

Provides requirements for post-approval changes submissions of biological products and other provisions
RDC 49/2011

Post-approval changes classified by risk

- Level 1 change (minor change)
- Level 2 change (moderate change)
- Level 3 change (major change)
Level 1 Changes

Immediate implementation

Refer to changes that have no impact on product’s quality

Usually included in pharmacopoeia or do not imply the need for analysis of the molecular structure
Biological Products
Current Regulation

**Level 2 Changes**

- Require prior approval from ANVISA
- Refer to changes that may impact on product quality and to modifications of non-compendial methodologies
- May imply the need of molecular structure analysis
- Molecular analysis has to be sufficient to demonstrate that the change does not affect product quality
Level 3 Changes

- Require prior approval from ANVISA
- Refer to changes that have great chances to impact the molecular structure and/or that leads to the need of conducting clinical trials: major complexity
- Usually implies the need to perform a new molecular characterization
- If analytical techniques indicate impact on the molecular structure or are insufficient to assess it: need for non-clinical and/or clinical trials
Comparability Exercise Guideline
Guideline for elaboration of Clinical Study Reports – Biological Products
Guideline for Non-clinical and clinical studies - Heparin Development by Comparability
Guideline for Non-clinical and clinical studies - Interferon Alpha Development by Comparability
Guideline for transport qualification of biological products
Future perspectives

1. Etanercept

2. Review the current guidelines
International Cooperation

- United States, Canada, China, Japan, Portugal, EMA, Cuba and Argentina
- PAHO – Pan American Health Organization
- WHO – World Health Organization
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THANK YOU

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