Developing Biologics: Understanding the Regulatory Pathways

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Director

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The Brazilian Health Surveillance Agency (Anvisa)

• Regulatory Agency: Administrative Independence and finance autonomy.

• Linked to the Ministry of Health.

• Management Contract (indicators and targets).

• Stability of the Directors (mandate).

• Board of Directors – 5 Directors named by the President of Republic, for a mandate of 3 years, renewed once for another 3 years.

• 16 years since its creation (Lei 9.782/1999).
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Anvisa Regulation Fields

- Foods
- Cosmetics
- Sanitizer
- Tobacco
- Pesticides
- Health Service
- Medicines
- Medical devices
- Official Laboratories
- Blood, Tissues and organs
- Pharmacovigilance
- Advertisement
- Ports, airports and borders
- International affairs
- SNVS coordination
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Organization Chart

Office of Biological Products

Agência Nacional de Vigilância Sanitária - Anvisa
<table>
<thead>
<tr>
<th>Biological Products</th>
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<tbody>
<tr>
<td>1. Vaccines</td>
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<tr>
<td>2. Hyperimmune sera</td>
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<tr>
<td>3. Blood products</td>
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<td>4. Biomedicines:</td>
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<tr>
<td>- medicines obtained from biological fluids or animal tissues; and</td>
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<tr>
<td>- medicines from biotechnological procedures.</td>
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<td>5. Monoclonal antibodies</td>
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<td>6. Medicines containing live, attenuated or dead microorganisms</td>
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<tr>
<td>7. Probiotics</td>
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<td>8. Allergens</td>
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Evolution of biological products regulation

- January
  - Law 9782 Anvisa

- November
  - RDC 323 Probiotics Requirements

- December
  - RDC 55 Update RDC 315/2005

- September 1976
  - Lei 6360 First Sanitary Surveillance legislation

- March 2002
  - RDC 80 Specifics Requirements for Biologicals

- August 2005
  - RDC 233 Allergenics Requirements
  - October
    - RDC 315 Update RDC 80/2002

- September 2009
  - RDC 49 Post-approval
  - RDC 50 Biologicals stability
Regulatory acts concerning biological products

- **RDC 46/00**
  - Blood products

- **RDC 71/09, RDC 168/02**
  - RDC 61/12
  - Label

- **RDC 81/08**
  - Import

- **RDC 234/05**
  - RDC 38/10
  - Quality control

- **RDC 17/10**
  - Good Manufacturing Practices

- **RDC 55/10**
  - Registration
  - RDC 49/11 e 24/13
  - Post-approval

- **Law 6360/76**
  - Decree 8.077/13

- **RDC 47/09 e 60/12**
  - Package insert

- **RDC 233/05**
  - Allergenics

- **RDC 323/03**
  - Probiotics

- **RDC 50/11 and 25/13**
  - Stability

- **RDC 81/08**
  - Import

- **Ordinance 174/96**
  - Antivenom serums
Biological products - Current regulation

RDC nº 55/2010

• **Biological product**: is the biological drug that is not new or is known, containing molecule with known biological activity, already licensed in Brazil and that has undergone all stages of manufacturing.

• **New Biological Product**: is the biological product containing molecule with known biological activity, not yet licensed in Brazil and that has undergone all stages of manufacturing.
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Biological products - Current regulation

RDC nº 55/2010

- New Biological Product
  - Complete dossier
  - Quality, Safety and Efficacy

- Biological product
  - Stand Alone Pathway
    - Complete dossier
  - Comparative clinical trials Phase III
  - Comparability Development Pathway
    - 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.
Transparency

- Drug Approval and Refusal Letters
  - Make drug letters available on Anvisa’s website.
  - Causes that lead a determined product to be approved or refused by Anvisa.
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

NEW!
International Cooperation

- United States, Canada, China, Japan, Portugal, EMA, Cuba and Argentina
- PAHO – Pan American Health Organization
- WHO – World Health Organization
- PMDA – Pharmaceuticals and Medical Devices Agency
THANK YOU!