Regional Regulations for Biotherapeutics

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BIO LATIN AMERICA
Conference

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Brazil
Regulatory Evolution:

Regulatory Requirements established since 2002

First Regulation for Biologic Products
- Non-Clinical Trials
- Clinical Trials

2002

Review of Regulation
- Clear requirements
- Requirements for post approval variations

2005

CHMP/437/04: Similar Biological Medicinal Product.
CHMP/42832/05: Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Non-Clinical and Clinical Issues.
CHMP/49348/05: Similar Biological Medicinal Products Containing Biotechnology-Derived Proteins as Active Substance: Quality Issues.

Second Review of Regulation
- Comparability and Individual pathway

2010

Specific guidelines by product

2011

Regulation for post approval variations
- Minor variations (HMP)
Regulation for stability studies and Specific Guidelines by product
Regulatory Environment:
Most Important regulations for Biologic Products

- RDC 55/10 MAA
- RDC 50/11 STABILITY
- RDC 49/11 POST APPROVAL
- Law 6.360/76 Dec. 8.077/13
- RDC 81/08 IMPORTATION
- RDC 234/05 LOCAL QC TESTING
- RDC 46/00 HEMODERIVATIVES
- RDC 47/09 PI/PIL
- RDC 71/09 PCL
- RDC 17/10 GMP
# Current biologics regulatory pathways:

*Clinical Trials Required for all pathways*

<table>
<thead>
<tr>
<th>Stages</th>
<th>Eval Type</th>
<th>Reg. Entity</th>
<th>I - Full</th>
<th>II - Comparable</th>
<th>III - Individual</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Clinical</td>
<td>ANVISA and AD HOCS</td>
<td>• Invitro / Invivo Pre-clinical studies</td>
<td>• Results of comparability studies according to ANVISA or International guidelines</td>
<td>• Does not require comparative tests on early development and initial clinical trials.</td>
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<td>• Efficacy / Safety Studies</td>
<td>• Reference products: approved by ANVISA through a full pathway</td>
<td>• Ph III has to be comparative (equivalence, non-inferiority or superiority trial).</td>
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<td>• Extrapolation of indication is possible</td>
<td>• Extrapolation of indication is not allowed</td>
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<td>• Immunogenicity Trial</td>
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<td>• Proposed PI/PIL aligned with clinical trial</td>
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<tr>
<td>II</td>
<td>CMC</td>
<td>ANVISA</td>
<td>• CMC Dossiers for DS and DP including full Manufacturing Process and QC testing validation</td>
<td>• Zone IVb Stability Studies, including stress stability study and transport validation</td>
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<td>• Packaging Artworks</td>
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<td>• CPP from manufacturing country</td>
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<td>Legal</td>
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<td>• GMP certificates issued by ANVISA</td>
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<td></td>
<td></td>
<td></td>
<td>• GMP issued by manufacturing country regulatory agency</td>
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