Legislation Perspectives in Brazil

The Brazilian regulatory system for Advanced Therapy Medicinal Products (ATMP) and the role and contribution of the Advanced Therapy Technical Committee-CAT

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I have no disclosures for the topics approached in this presentation
To protect population health

Minimizing health risks related to production and use of goods and services

To promote population health

Expand access to goods and services that improve health and life quality for the population
Advanced Therapy Medicinal Products - ATMP

DEPARTMENT OF BLOOD, TISSUES, CELLS, ORGANS AND ATMP
Brazilian Regulatory Framework for ATMP

Conventional Therapy

- minimally manipulated cells, tissues, organs and intended for homologous use only.
  - Tissues and cells for reproductive use
  - Blood and components for transfusion
  - Hematopoietic progenitor cells for bone marrow transplantation
  - Tissues and organs for transplants

Advanced therapy

- substantially manipulated cells or tissues or cells intended to exert a different function (not intended to be used for the same essential function in our body)
  - Somatic cell therapy products
  - Tissue engineered products
  - Gene therapy products (in vivo and ex vivo)

Risk-based approach
Advanced Cell Therapy Products: contains or consists of cells or tissues that have been subjected to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, or of cells or tissues that are not intended to be used for the same essential function(s) in the recipient and the donor;

Gene Therapy Product: it contains an active substance which contains or consists of a recombinant nucleic acid used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence.
Brazilian Regulatory Framework for ATMP

Starting Material (blood, tissues, cells)

Substantial manipulation or new function

yes

Gene Therapy (ex or in-vivo)

no

Conventional products/services (transfusion/transplants)

Avanced Therapy Medicinal Products

Non Clinical

Clinical Trial

Marketing Authorization

GLP

RDC 260/2018

CP 706/19

Post-Market monitoring

Ethics Comitee

GMO analysis

CTNBio

Good Manufacturing Practices – RDC 214/2018
Brazilian Regulatory Framework for ATMP

Minimally manipulated with innovation in original biological function

- Substantially manipulated
- Tissue engineering
- Genes

Risk Approach
Brazilian Regulatory Framework for ATMP

Marketing Authorization – under public consultation

Development

Non-clinical

Pre Submission meeting

Pre Classificacion ATMP

Clinical Trials

“conditional” marketing authorization (requires additional data on efficacy)

Marketing Authorization (CLASS II)

Simplified Marketing Authorization (CLASS I)

approved clinical trials

Good Manufacturing Practices

Biopharmacovigilance
# Brazilian Regulatory Framework for ATMP

## Regulatory Classification as ATMP – Anvisa with support of CAT

### CLINICAL TRIALS

<table>
<thead>
<tr>
<th>ATMP CLASS I</th>
<th>ATMP CLASS II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Trial</strong> application (Simplified)</td>
<td><strong>Clinical Trial</strong> application (Complete)</td>
</tr>
<tr>
<td>Start of the study with submission application</td>
<td>Approval of Anvisa to start study</td>
</tr>
<tr>
<td>Approval in Ethics Committee (CEP/CONEP)</td>
<td>Approval in Ethics Committee (CEP/CONEP)</td>
</tr>
<tr>
<td>Monitoring by risk-based inspection program</td>
<td>Biosafety Commission (CTNBio) for Gene Therapy</td>
</tr>
<tr>
<td></td>
<td>Monitoring by risk-based inspection program</td>
</tr>
</tbody>
</table>
Brazilian Regulatory Framework for ATMP

CLINICAL TRIALS APPLICATION - CTA
RDC n. 260/2018

- Investigator’s Brochure;
- Clinical Trial protocol;
- Investigational ATMP Dossier: quality, manufacture and control, and data from non-clinical and clinical studies.

Class I products = study can be started after submission

180 days = class II products
Current Clinical Trials Application with ATMP in Brazil

- **3 Clinical Trials approved**
  - Gene Therapy \textit{in vivo}
  - Cell Therapy (substantial manipulation)
  - Global Sponsors

- **5 Clinical Trials ongoing**
  - Under monitoring
  - Advanced Cell Therapy
  - National Sponsors

- **1 Clinical Trial not approved**
  - Gene Therapy \textit{in vivo}
  - Global Sponsor

- **5 Clinical Trials under analysis**
  - 3 Gene Therapy
  - 2 Cell Therapy

- Anvisa’s response time: 73 – 120 days

- **subjects**
  - oftalmology, hematology, oncology, orthopedy
Marketing Authorization – under public consultation (CP 706/18)

- Report on non-clinical studies
- Report on clinical trials
- Chemistry, Manufacturing and Control (Quality data)
- Pos-marketing
- GMP production

Simplified Registration

Complete Registration
Rare diseases

Emerging or re-emerging diseases

Public health emergencies or severe debilitating conditions

Diseases for which there is no therapeutic alternative available in Brazil

120 days
Brazilian Regulatory Framework for ATMP Subject to Conditional Marketing Authorization that Requires Additional Data Monitoring

CONDITIONS:

I – Use in severe debilitating conditions;

II – Use in situations where there is no available therapy, product or comparable alternative medicine for the disease stage;

III – Where there is solid evidence for a significant improvement in patient condition or disease remission

DOCUMENTS:

- Report on Non-clinical Studies
- Report on Clinical Trials already performed
- Schedule of the ongoing/planned Clinical Trial
- Disease description/ Relevance
- Medicine leaflet informing conditions to professionals and patients

- Development plan
- Specific Obligations
- Valid for 1 year, up to 5 years
Authorization for ATMP products
not requiring marketing authorization application

- ATMP produced under **non-routine conditions** for a **specific patient**, under the responsibility of a medical doctor, prepared according to defined quality and safety conditions;

- This only applies to patients with indication of use of the ATMP for the treatment of **diseases without therapeutic alternative available in the country** and under **imminent life risk condition**;

- Anvisa’s authorization informing the rationale for the use of the ATMP and the previous clinical experience with the product, as well as information on non-clinical and clinical data available;

- Commercialization is prohibited;

- Clinical follow-up report to ANVISA;

- **GMP certification of the production center**
GLOBAL MARKETING AUTHORIZATION FOR ATMP

BRASIL 2019
1 ATMP submission
(hereditary retinal distrophy: under analysis)
REGULATORY CONVERGENCE

EMA: European Medicines Agency

FDA: U.S Food and Drugs Administration

PMDA: Pharmaceuticals and Medical Devices Agency

IPRP - International Pharmaceutical Regulators Programme

ICH - INTERNATIONAL COUNCIL FOR HARMONISATION
The contribution of the Advanced Therapy Technical Committee-CAT in the development of ATMP regulation in Brazil

- Specialized Committee composed by professionals with technical expertise in the area (Cell and Gene Therapy);
- Members of universities and research institutes;
- 7 members designated and confirmed by Anvisa’s board of Directors;
- Sign confidentiality and conflict of interest terms;
- 3 years mandate (can be renewed);
The contribution of the Advanced Therapy Technical Committee-CAT in the development of ATMP regulation in Brazil


- Assist Anvisa in preparation of technical documents and guidances;

- Assist Anvisa’s team in reviewing Clinical Trial and Marketing Authorization Application;

- Confirm if a product which is based on genes, cells or tissues, meets the scientific criteria for defining an ATMP (Classification).
CAT Perspectives

- Contribute to a qualified analysis of dossiers submitted to Anvisa;
- Promote scientific advice to national producers;
- Train Anvisa’s staff to work with the product;
- Ensure qualified Agency evaluation responses;
- Transform Anvisa as a reference in the area for Latin America.
CAT Perspectives

- Anvisa is establishing a network of experts (RENETA) to help evaluating new submissions;
- CAT members will form part of the network and help training new members;
- CAT will help to resolve divergencies and to set the framework for new therapies;
Thanks for your attention and ANVISA for help with the presentation

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