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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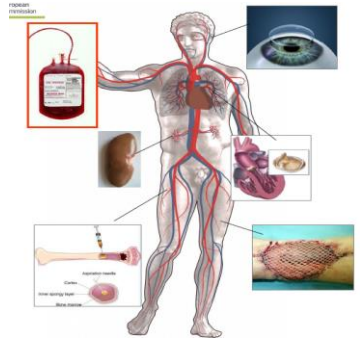
I have no disclosures for the topics approached in this presentation



National Health Brazilian Agency - ANVISA

NATIONAL HEALTH REGULATORY AGENCY

To protect population health

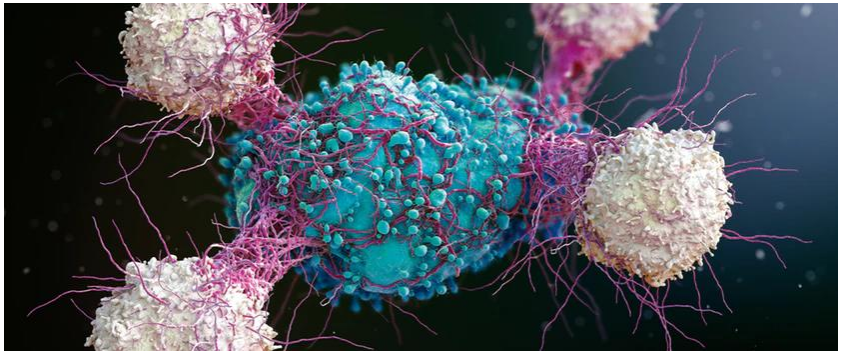
Minimizing health risks related to production and use of goods and services

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

risk-based approach

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*)

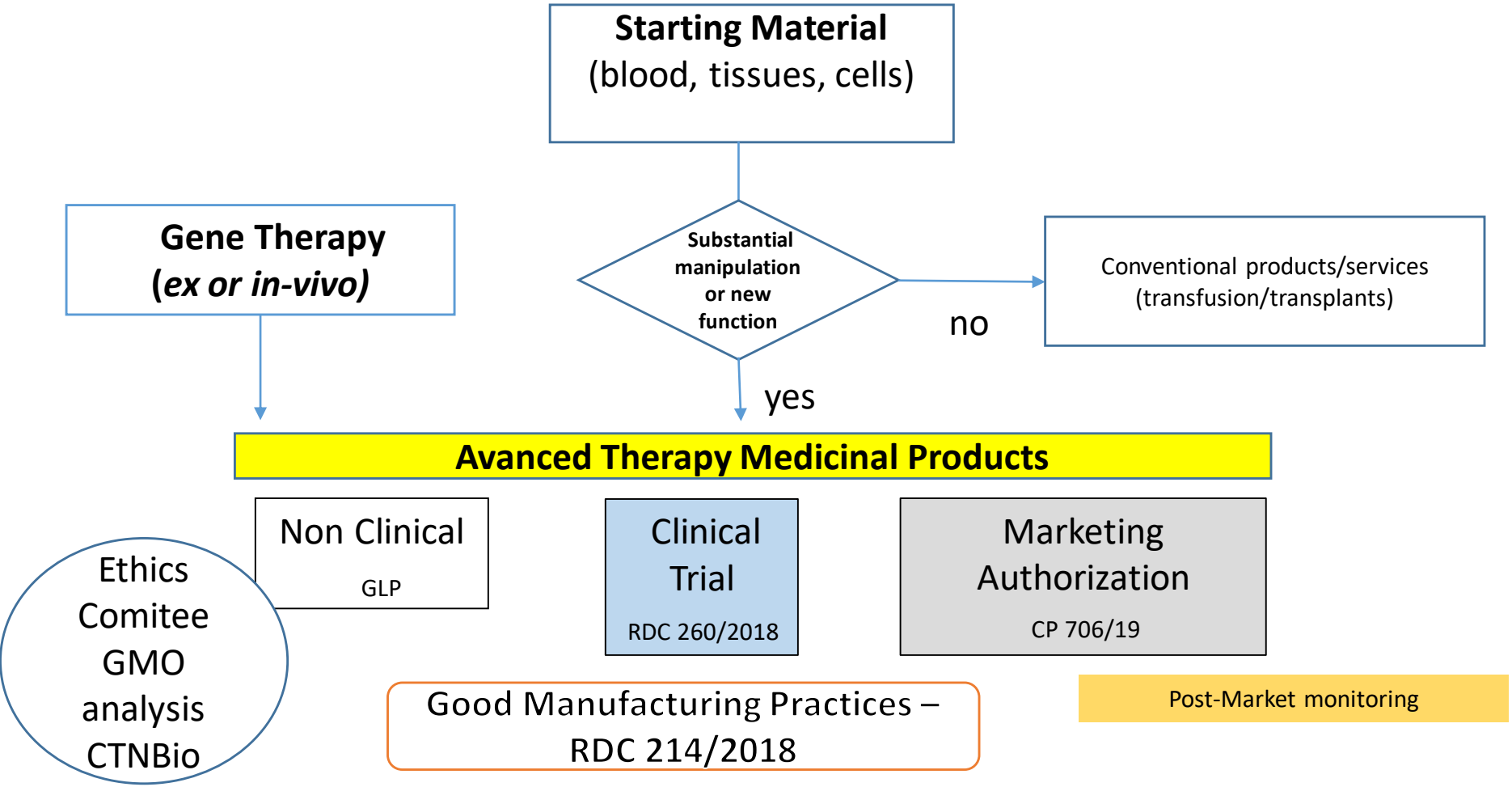
Cells

Genes

- ✓ 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

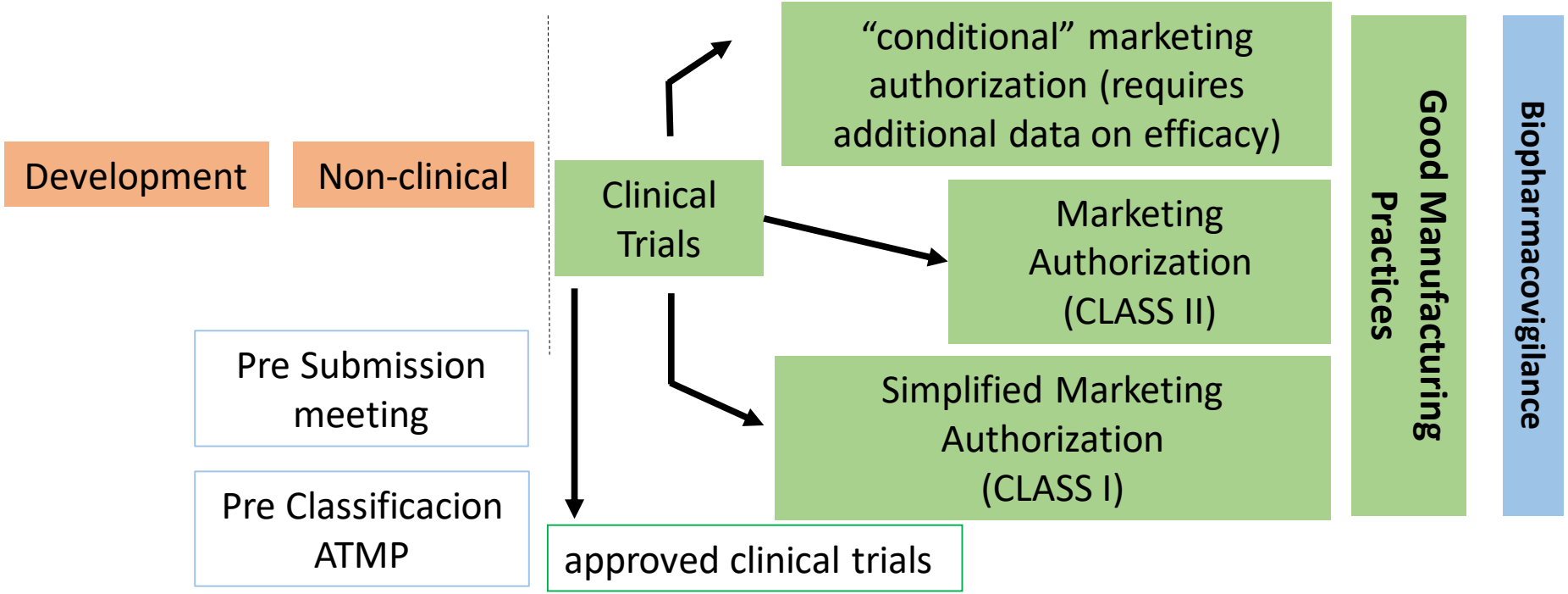


Brazilian Regulatory Framework for ATMP

RISK APPROACH

Brazilian Regulatory Framework for ATMP

Marketing Authorization – under public consultation



Brazilian Regulatory Framework for ATMP

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

CLINICAL TRIALS

ATMP CLASS I	ATMP CLASS II
Clinical Trial application **(**Simplified**)**	**Clinical Trial** application **(**Complete**)**
Start of the study with submission application	Approval of Anvisa to start study
Approval in Ethics Committee (CEP/CONEP)	Approval in Ethics Committee (CEP/CONEP)
	Biosafety Commission (CTNBio) for Gene Therapy
Monitoring by risk-based inspection program	Monitoring by risk-based inspection program

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

Anvisa's response time: 73 – 120 days

12

3 Clinical Trials approved
Gene Therapy *in vivo*
Cell Therapy (substantial manipulation)
Global Sponsors

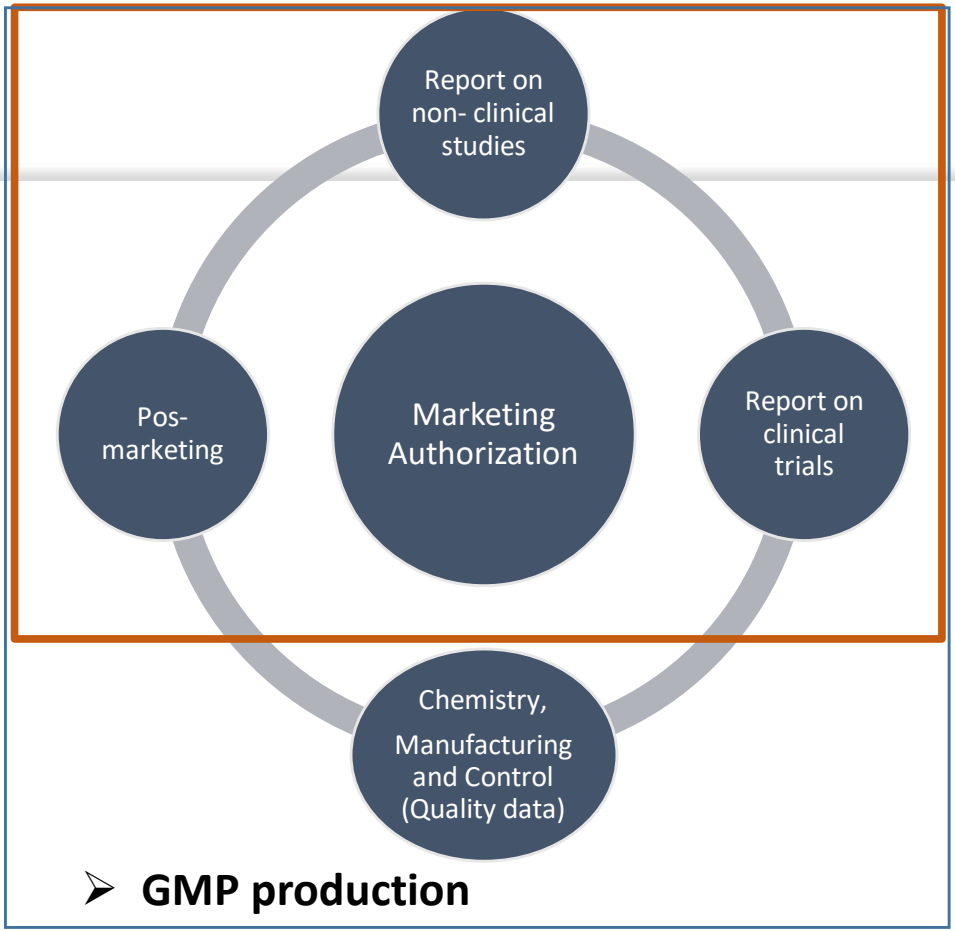
5 Clinical Trials ongoing
Under monitoring
Advanced Cell Therapy
National Sponsors

1 Clinical Trial not approved
Gene Therapy *in vivo*
Global Sponsor

5 Clinical Trials under analysis
3 Gene Therapy
2 Cell Therapy

oftalmology,
hematology
oncology,
orthopedy

Marketing Authorization – under public consultation (CP 706/18)



Simplified Registration

Complete Registration

Brazilian Regulatory Framework for ATMP Subject to Accelerated Approval

120 days

- 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

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 analisys)

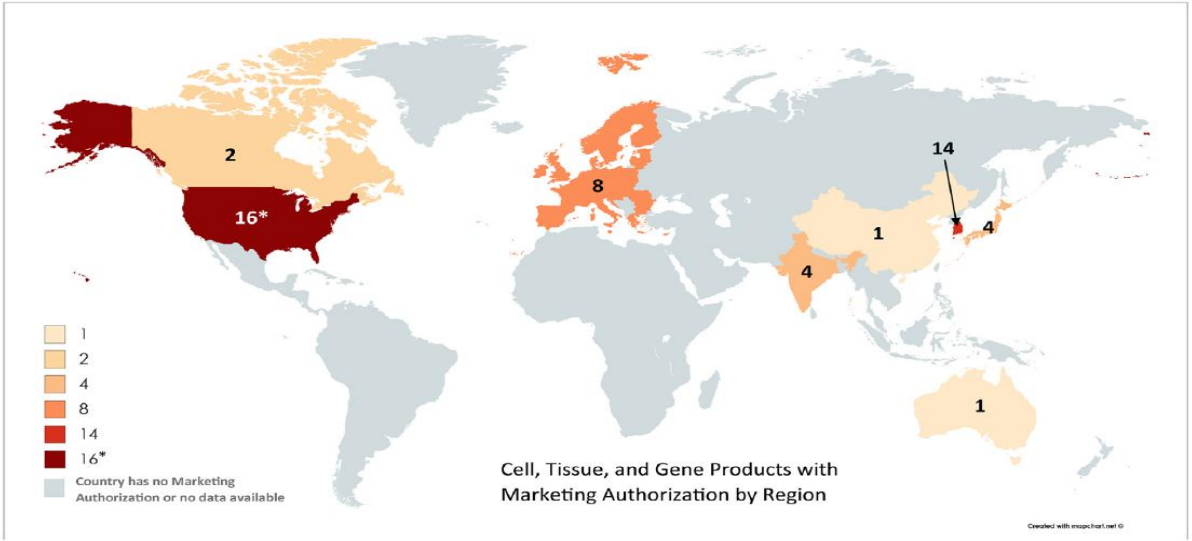


Figure 1. Number of cell, tissue and gene products with MA per region. *Eight products based on cord blood hematopoietic progenitors for unrelated donor hematopoietic progenitor cell transplantation have been included in the US's total number. These hold a MA license only in the US. Similar products are available in most countries as cell transplants and not as marketed products. The number of products presented in this figure does not include either products with Regenerative Medicine Advanced Therapy (RMAT) designation (United States Food and Drug Administration [USFDA]) or products with suspended MA.

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

- Contribute with Anvisa's regulation in ATMP: regulation in GMP (RDC n. 214/2018), Clinical Trials (RDC n. 260/2018) and ATMP aplication on Marketing Authorization (Public Consult n.706/2019).

- Assist Anvisa in preparation of technical documents and guidances;

- Assist Anvisa's team in reviewing Clinical Trial and Marketing Authorization Aplication;

- 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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