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COMISSÃO TÉCNICA INTEGRANTE DO MCTI

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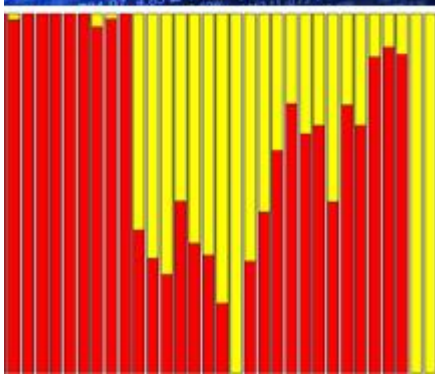
GOVERNO FEDERAL



Familiarity – what can we learn from what we already know?

Drawing from: experience with biotech plants, "conventional" food safety, animal breeding/sequencing data

4th International Workshop on Regulatory Approaches for Agricultural Applications of Animal Biotechnologies

September 13th, 2022 – São Roque – Brazil

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ZGC
Zebu Genome Consortium

Evolution of Science

- Scientific innovations are daily incorporated to technological repertoire;
- Regulation follows scientific progress;
- It is impossible to “de-invent” something;
- Unlimited innovative capacity: science main feature;
- 2020 Chemistry Nobel Prize on CRISPR.

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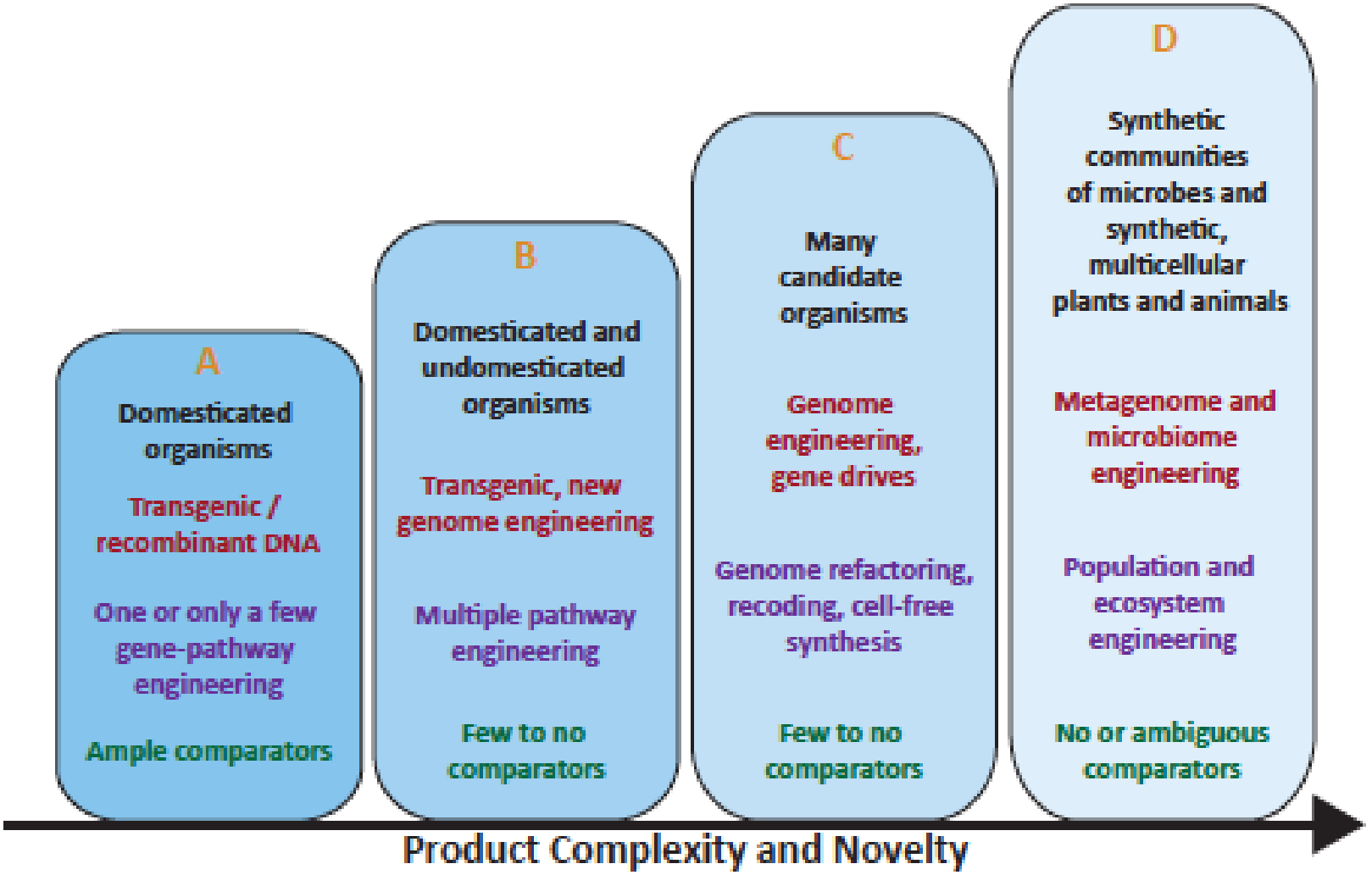

National Academies of Sciences, Engineering, and Medicine 2017. Preparing for Future Products of Biotechnology. Washington, DC: The National Academies Press. https://doi.org/10.17226/24605.

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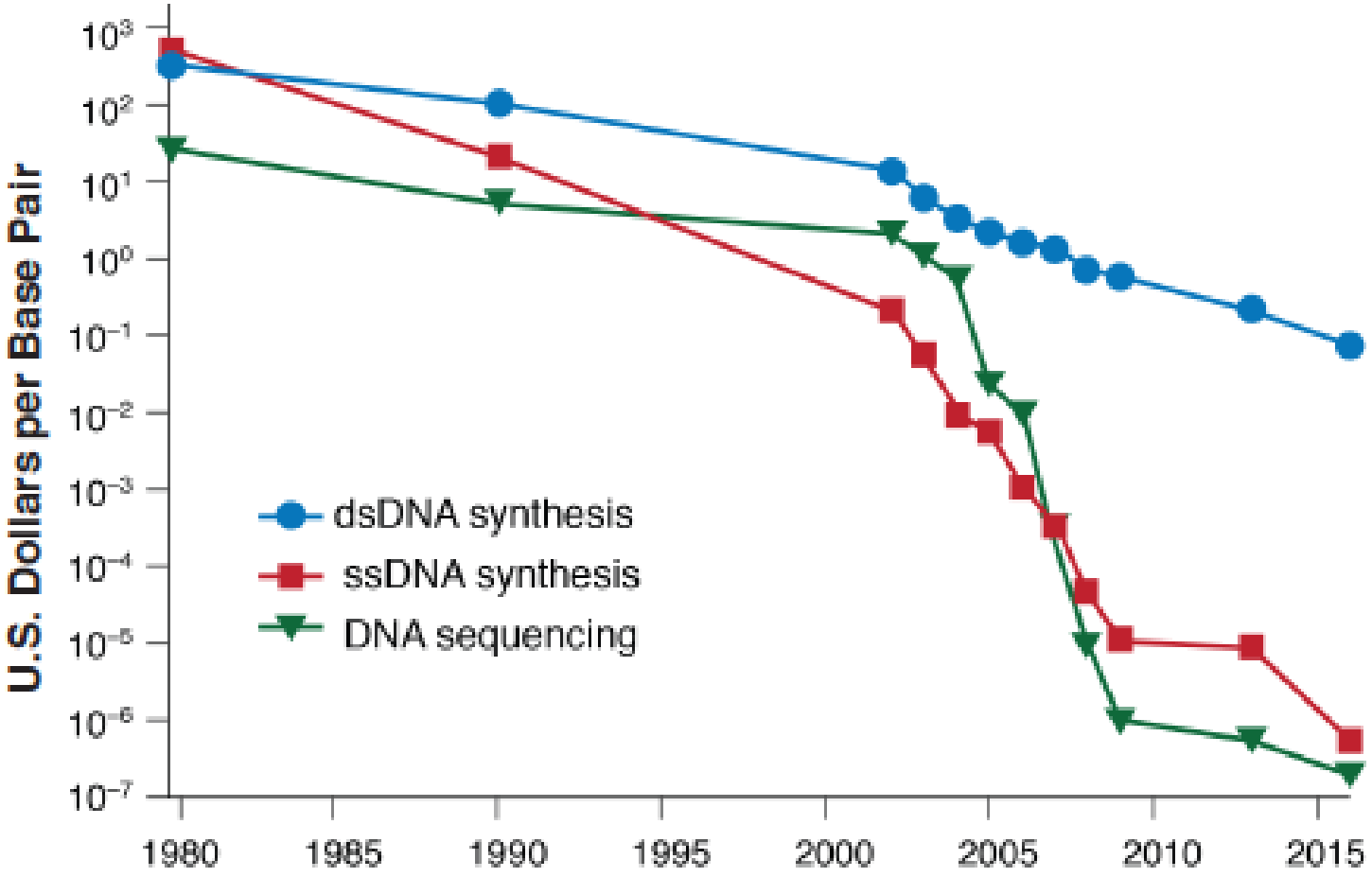

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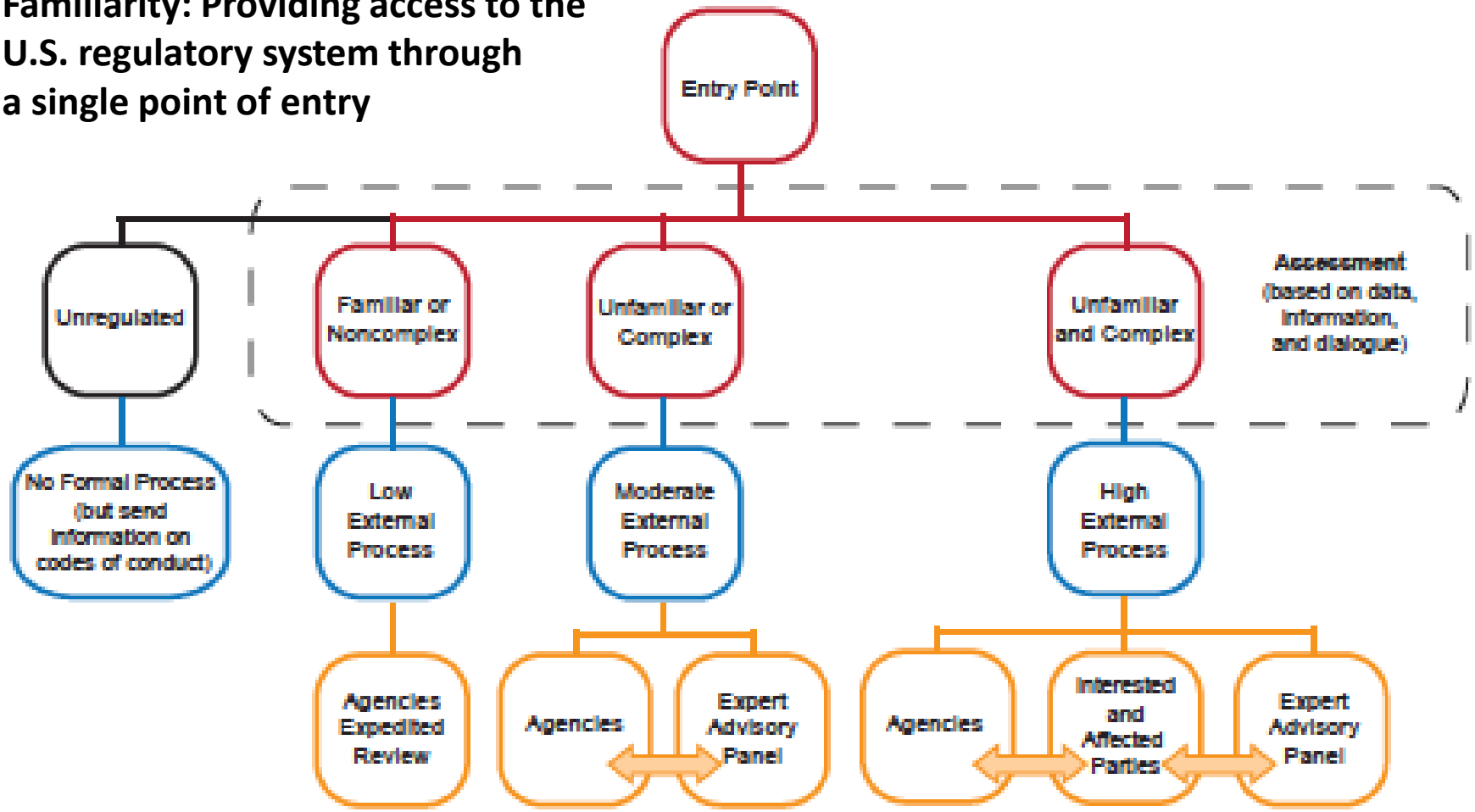
Familiarity: Providing access to the U.S. regulatory system through a single point of entry



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Brazilian Biosafety Regulation

Historical contextof NBTs / Genome Edit Animals

1995
Federal Law 8.974
- Biosafety Law
- First GMO regulation

1998
First GMO Commercial Approval
- Roundup Ready Soybean

2004
Scenarium
- No other GMO product got commercial licence
- Biosafety legislation proved to be nonfunctional

2005
Law 11.105/2005
Second Biosafety Law

2006
- **Normative Resolution Nº 1**
- **Normative Resolution Nº 2**

2007
- **Normative Resolution Nº 4**

2008
- **Normative Resolution Nº 5**

2009
Scenarium
- 19 GM Plants Comercial Approval
- First GM Microorganism Commercial Approval Request - Strain Y1979 – Amyris

2015
Experts Working Group
- Elaboration of specific rules for consult for NBTs

2018
Normative Resolution Nº 16
Specific rules for consult for NBTs

2018
First consults of microorganisms
First consults of plants
First consults of animals
First consult of vaccines (canine)

1995 - 2005 | 2005 - 2009 | 2010 - 2018

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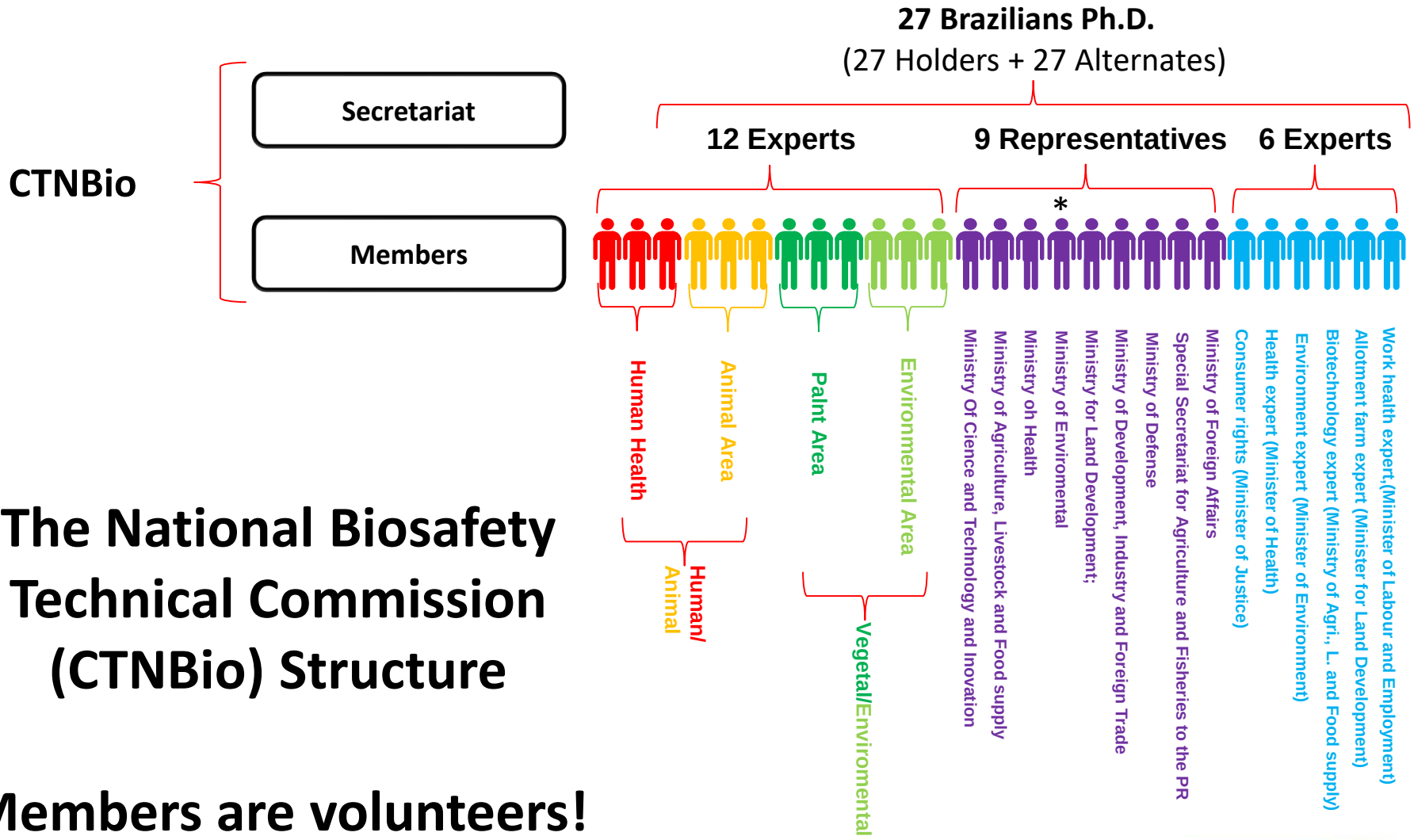

The National Biosafety Technical Commission (CTNBio) Structure

Members are volunteers!

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CTNBio Two "Chambers" – Day 1

Human and Animal

- Vacines
- Livestock
- Drugs

Plant and Environment

- Crops
- Trees
- Microbes

- Lab Certification (CQB)
- Project Analysis (NB2 up)
- Field Trial approval
- Commercial approval
- Gene Editing consultation
- Product risk analysis
- Any other relevant analysis
- Technical visits

Monthly two-day meeting

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CTNBio Plenary – Day 2

Ratifies or re-discuss previous day decisions from the "chambers"

Revise decisions, if necessary, issue new guidelines

Give publicity of the results of biosafety analysis

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CTNBio Activities

GMO Commercial Aprovals

The total number of commercial approvals of GMOs in Brazil are: 104 genetically modified plants (55 maize, 22 cotton, 18 soybean, 6 sugarcane, 2 eucalyptus and 1 common bean), 56 recombinant vaccines, 1 genetically modified mosquito, **1 genetically modified fish (Salmon)** and 43 genetically modified microorganisms, and derivatives.

(http://ctnbio.mctic.gov.br/liberacao-comercial#/liberacao-comercial/consultar-processo)

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CTNBio motivation in 2015

- Need to evaluate the *"Precision Breeding Innovation"* (PBI) approaches
- Involving the *"New Breeding Technologies*" – NBTs
- Framed on the legal definitions of Law 11.105/2005 (Biosafety Act)

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Normative Resolution Nº 16
Técnicas Inovadoras de Melhoramento Genético - TIMP (PBI)

Resolução Normativa Nº 16, de 15 de janeiro de 2018

Imprimir

Estabelece os requisitos técnicos para apresentação de consulta à CTNBio sobre as Técnicas Inovadoras de Melhoramento de Precisão

A COMISSÃO TÉCNICA NACIONAL DE BIOSSEGURANÇA – CTNBio, no uso de suas atribuições legais e regulamentares e em observância às disposições contidas nos incisos XV e XVI do art. 14 da Lei nº 11.105, de 24 de março de 2005;

CONSIDERANDO a necessidade de avaliar as Técnicas Inovadoras de Melhoramento de Precisão (TIMP), do inglês Precision Breeding Innovation (PBI) e que também englobam as denominadas Novas Tecnologias de Melhoramento, do inglês New Breeding Technologies -NBTs, à luz dos preceitos previstos na Lei nº 11.105, de 24 de março de 2005;
Considerando que a Lei nº 11.105, de 2005, define moléculas de ADN/ARN recombinante, engenharia genética e organismo geneticamente modificado - OGM nos incisos III, IV e V de seu art. 3º, respectivamente;

Considerando que as TIMP abrangem um conjunto de novas metodologias e abordagens que diferem da estratégia de engenharia genética por transgenia, por resultar na ausência de ADN/ARN recombinante no produto final;

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TIMP/PBI

- TIMP/PBI encloses a group of new methodologies and approaches which differ from transgenic genetic engineering, **by resulting in the absence of recombinant DNA/RNA in the final product;**
- Legal definition of GMO is at the Article 3rd of the Biosafety Act (2005)

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Biotechnological Novelties

Early flowering
Seed Production Technology
Reverse Breeding
RNA-dependent DNA methylation
Site-Directed Mutagenesis
Oligonucleotide Directed Mutagenesis
Agroinfiltration / agroinfection
Topical/systemic use RNAi
Viral vector
Others

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Normative Resolution Nº 16

Consultation Letter:

Asking if the PRODUCT (animal, plant, seed, semen, embryo, grain, meat, milk, vaccine, microorganism, etc) generated by TIMP/PBI is framed in the legal definition of GMO (or derivatives) or not

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1. With regard to the original organism (Parentals), inform:

1.1 The identification of the **genetic technology**, purpose and intended use of the resulting organism and its derivatives;
1.2 The **taxonomic classification**, from family to the most detailed level of the organism to be released, including, when appropriate, subspecies, cultivar, patovar, strain and serotype;
1.3 The **risk classification** of the genetically modified organism in accordance with Normative Resolution No. 2 of November 27, 2006
1.4 The **gene** (s) and / or **genetic element** (s) **handled**, the organism (s) of origin and their specific functions, where applicable
1.5 The **genetic strategy** (s) used to produce the desired modification (s); the genetic map (s) construction (s) used in the process indicating, with all genetic elements present;
1.6 The **molecular characterization** of the result of manipulation in the recipient organism (parent and final product), where applicable, providing information related to: (1) number of manipulated copies (e.g. number of genomic sequences, number of copies alleles, etc.); (2) location in the genome of the manipulated region, when possible; (3) identify the presence of genetic modifications off-target, where applicable.
1.7 The **product of expression** of the manipulated genomic region (s), described in detail, where applicable.

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2 With regard to the product (offspring, lineage or final product) inform:

2.1 **Proof of the absence of recombinant DNA / RNA molecules**, through the use of molecular methods.
2.2 Whether the product containing DNA / RNA molecules for topical / systemic use has the **recombinant ability to enter into the target species** and / or non-target species.
2.3 Whether **the product** covered by the application **is commercially approved** in other countries.
2.4 If **the product uses the principle of gene drive** (gene drive) that may allow the phenotypic change has the potential to spread throughout the population of the recipient organism, to spell out the using at least two different strategies.
2.5 **How was evaluated the possibility of possible unintentional (off-target) effects** of the technology product.

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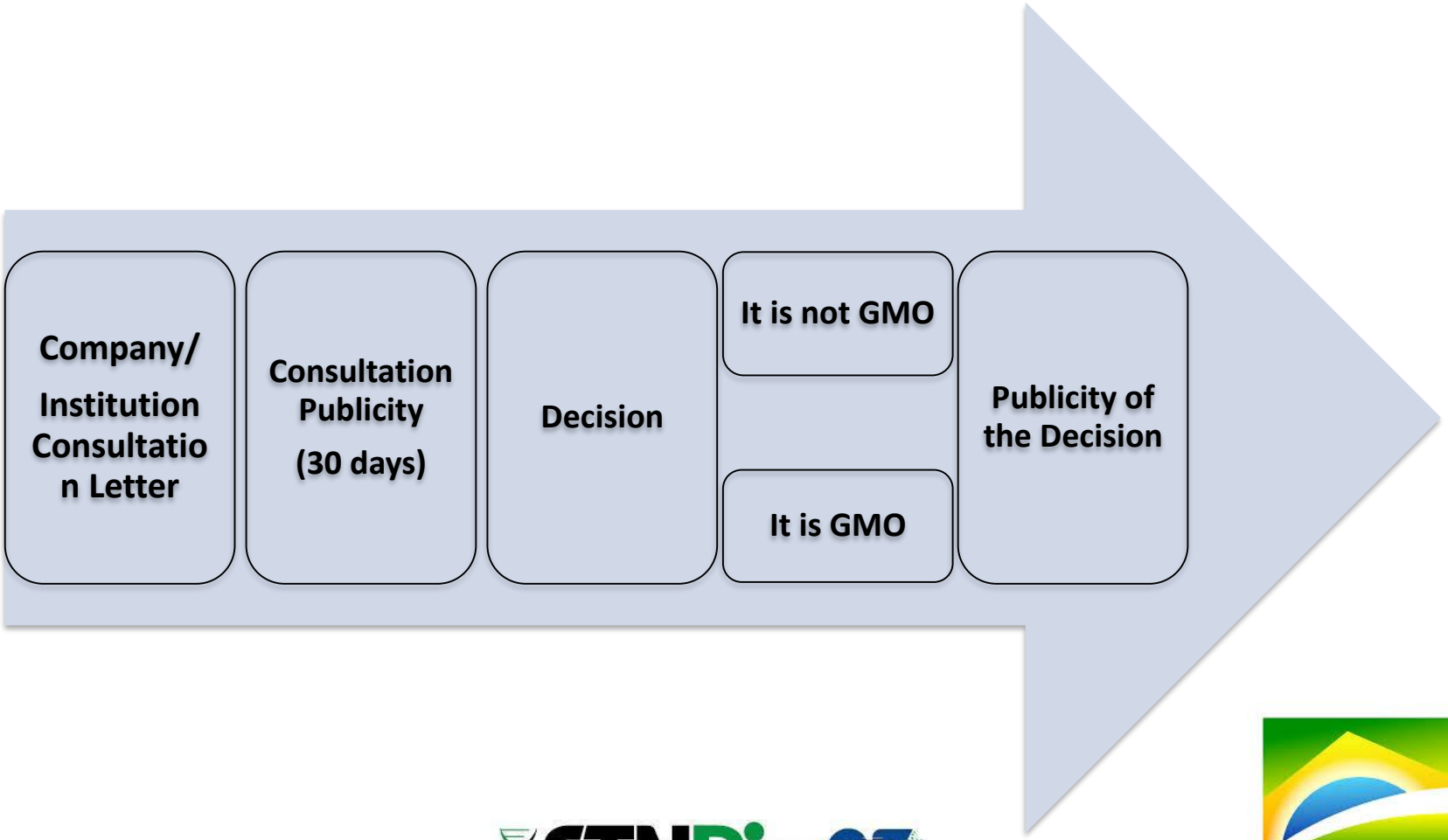
Normative Resolution Nº 16
Procedures



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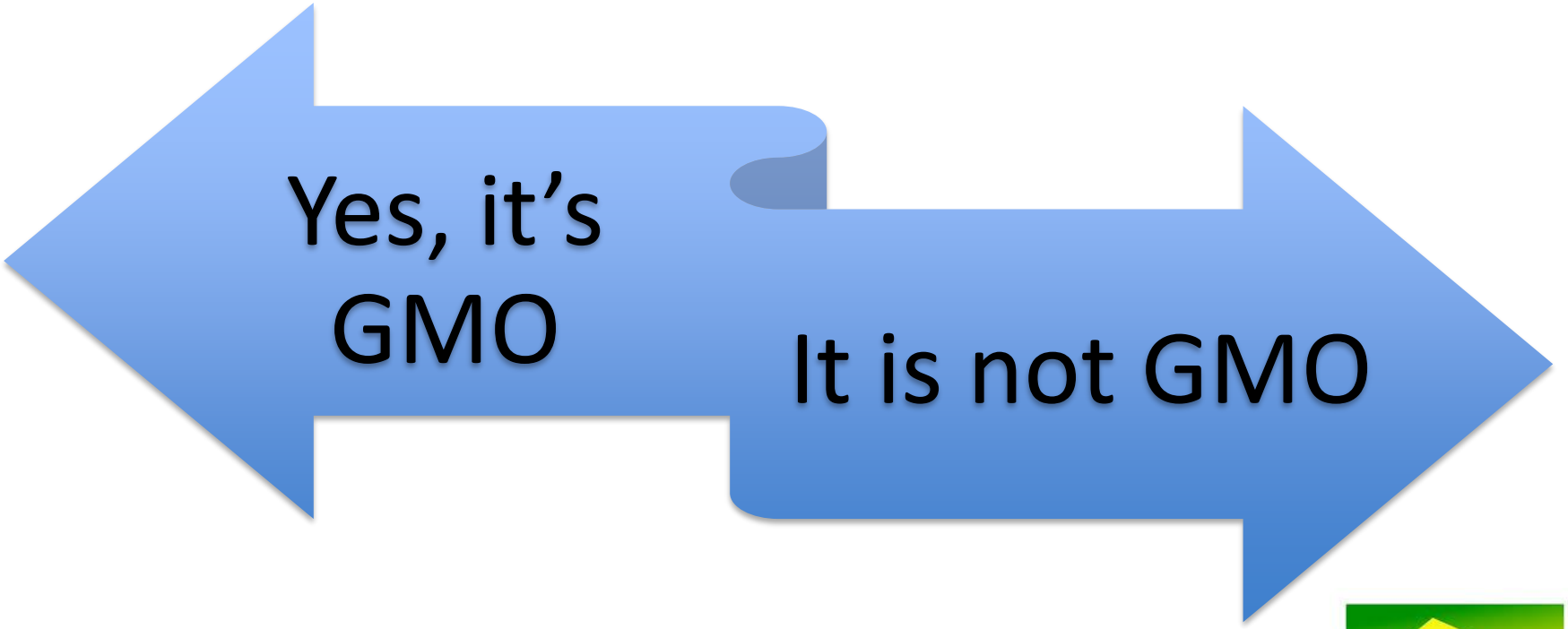
Normative Resolution Nº 16
CTNBio Decision



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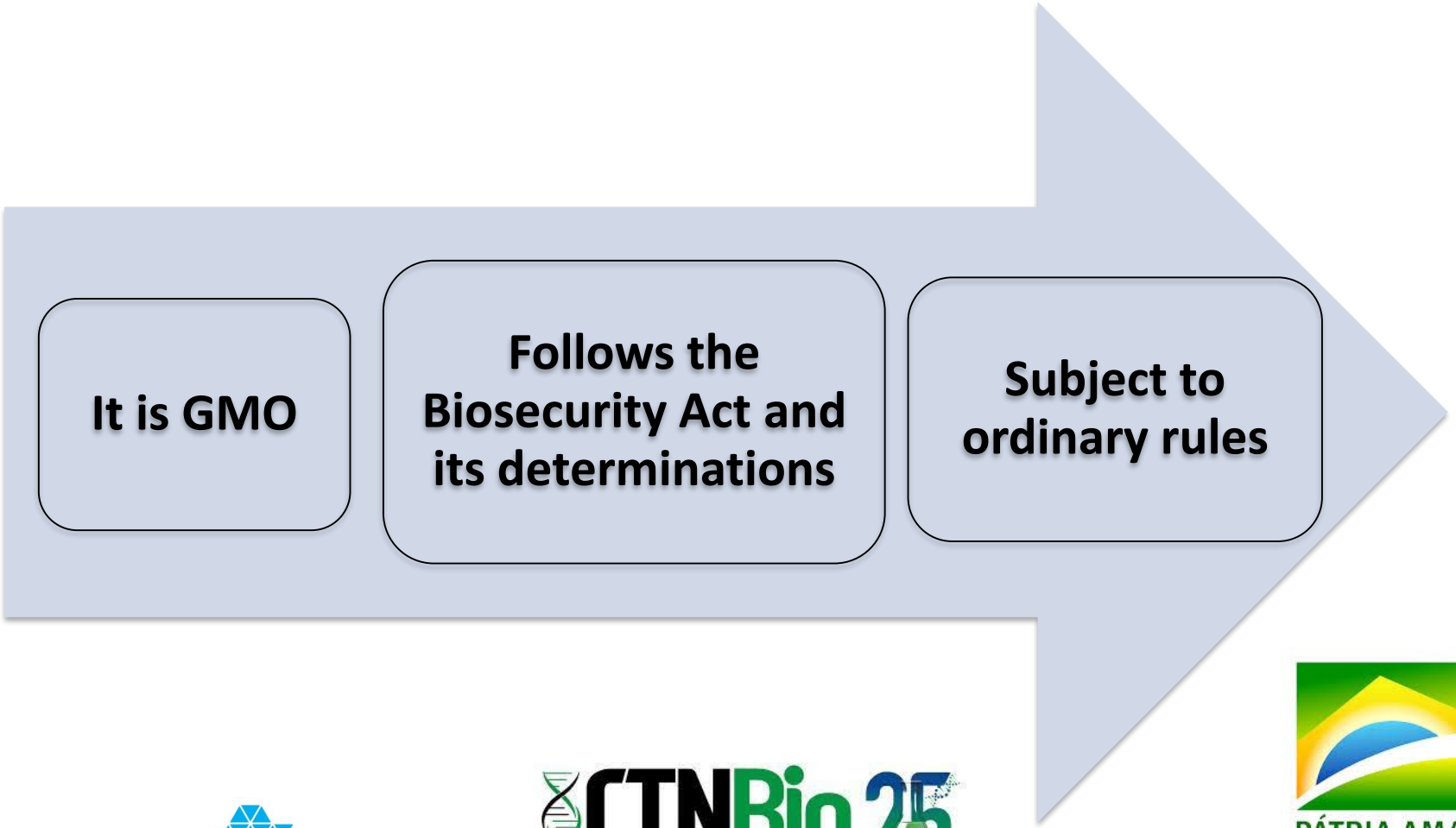
Normative Resolution Nº 16
CTNBio Decision: It is GMO



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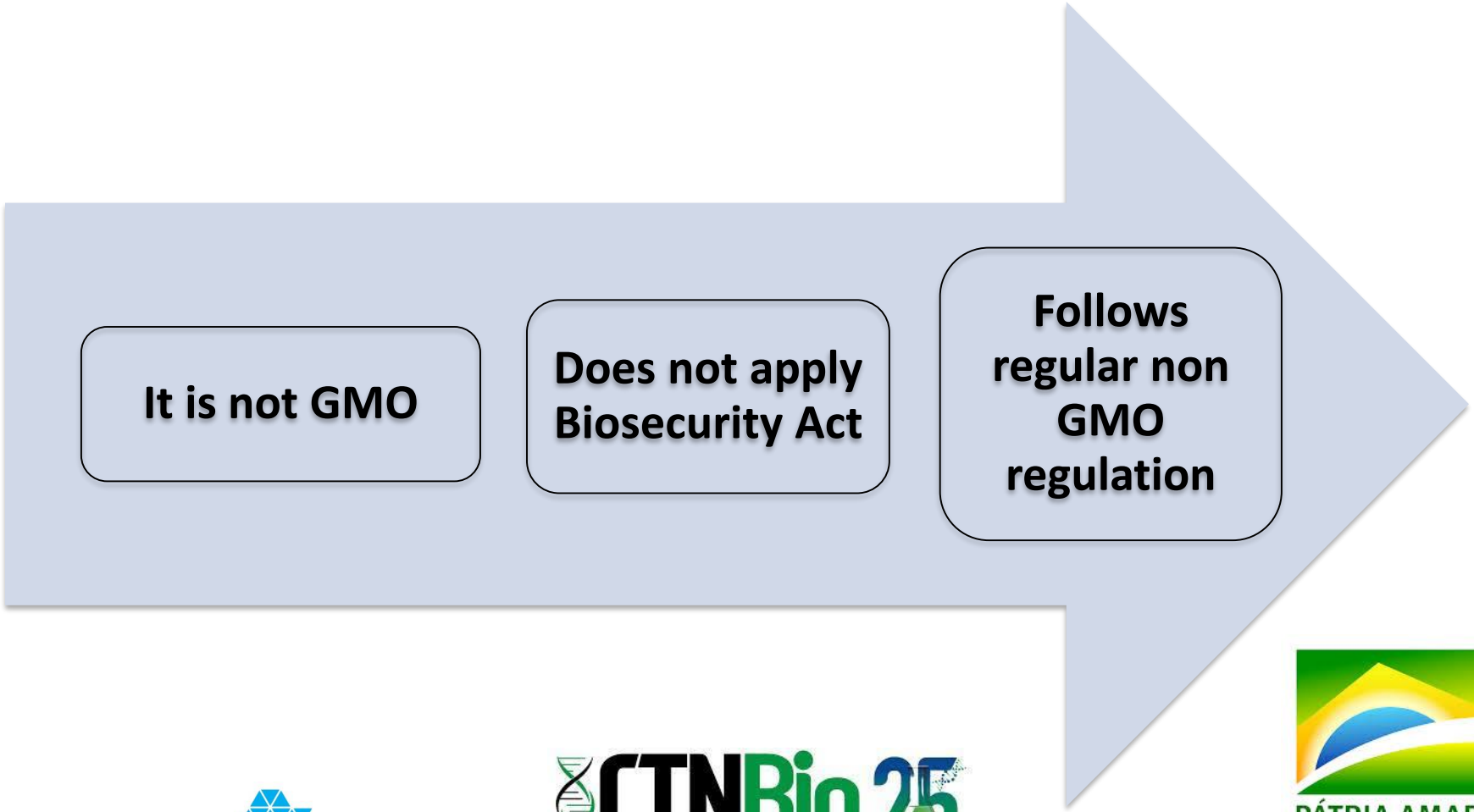
Normative Resolution Nº 16
CTNBio Decision: It is not GMO



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Normative Resolution Nº 16
CTNBio Principles

Prior inquire on the legal framework of the product

Parental and Product descriptions

Description of the technique (s) employed

Precaution with “Gene drive”

Attention to “off target” effects

Analysis “case-by-case”

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Normative Resolution Nº 16
Recent Cases approved as Non GMO

- *Spodoptera frugiperda* and *Helicoverpa armigera*, insects that attack cultivated crops with genes silenced;
- Lines of *Saccharomyces cerevisiae*;
- **Bull semen with increased muscle;**
- Strain of *Bacillus thuringiensis*;
- Covid 19 vaccine;
- Acetolactate synthase (ALS) inhibitor herbicides tolerant soybean;
- Nematode control with proteins from genus *Bacillus*;
- **Angus cattle for genome edition for slick**
- Sugar cane modified with the CRISPR/Cas9
- Tilapia with muscular hypertrophy (myostatin)

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Review > Transgenic Res. 2022 Apr;31(2):167-199. doi: 10.1007/s11248-021-00294-3.
Epub 2022 Jan 9.

Towards progressive regulatory approaches for agricultural applications of animal biotechnology

Eric M Hallerman [1], Justin P Bredlau [2], Luiz Sergio A Camargo [3], Maria Lucia Zaidan Dagli [4], Margaret Karembu [5], Godfrey Ngure [5], Rhodora Romero-Aldemita [6], Pedro Jesús Rocha-Salavarrieta [7], Mark Tizard [8], Mark Walton [9], Diane Wray-Cahen [2]

Affiliations + expand

PMID: 35000100 PMCID: PMC8742713 DOI: 10.1007/s11248-021-00294-3

Free PMC article

Organisation for Economic Co-operation and Development

ENV/CBC/MONO(2022)23

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English - Or. English

21 July 2022

ENVIRONMENT DIRECTORATE
CHEMICALS AND BIOTECHNOLOGY COMMITTEE

Development in Delegations on Biosafety Issues, April 2021 – May 2022

Series on the Harmonisation of Regulatory Oversight in Biotechnology
No.71

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Thank You!

fernando.garcia@unesp.br

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