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Genome Editing in Latin America: Regional Regulatory Overview

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Publication design by Patti Mulligan

DOI: http://dx.doi.org/10.18235/0003410

Genetic Engineering and Society Center, NC State University

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JULY 2021

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Foreward

The power and promise of genome editing, CRISPR specifically, was first realized with the discovery of CRISPR loci in the 1980s.[3] Since that time, CRISPR-Cas systems have been further developed enabling genome editing in virtually all organisms across the tree of life.[3] In the last few years, we have seen the development of a diverse set of CRISPR-based technologies that has revolutionized genome manipulation.[4] Enabling a more diverse set of actors than has been seen with other emerging technologies to redefine research and development for biotechnology products encompassing food, agriculture, and medicine.[4] Currently, the CRISPR community encompasses over 40,000 authors at 20,000 institutions that have documented their research in over 20,000 published and peer-reviewed studies.[5] These CRISPR-based genome editing tools have promised tremendous opportunities in agriculture for the breeding of crops and livestock across the food supply chain. Potentially addressing issues associated with a growing global population, sustainability concerns, and possibly help address the effects of climate change.[4] These promises however, come along-side concerns of environmental and socio-economic risks associated with CRISPR-based genome editing, and concerns that governance systems are not keeping pace with the technological development and are ill-equipped, or not well suited, to evaluate these risks.

The Inter-American Development Bank (IDB) launched an initiative in 2020 to understand the complexities of these new tools, their potential impacts on the LAC region, and how IDB may best invest in its potential adoption and governance strategies. This first series of discussion documents: "Genome Editing in Latin America: Regulatory Overview," and "CRISPR Patent and Licensing Policy" are part of this larger initiative to examine the regulatory and institutional frameworks surrounding gene editing via CRISPR-based technologies in the Latin America and Caribbean (LAC) regions. Focusing on Argentina, Bolivia, Brazil, Colombia, Honduras, Mexico, Paraguay, Peru, and Uruguay, they set the stage for a deeper analysis of the issues they present which will be studied over the course of the next year through expert solicitations in the region, the development of a series of crop-specific case studies, and a final comprehensive regional analysis of the issues discovered.

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I. INTRODUCTION[i]

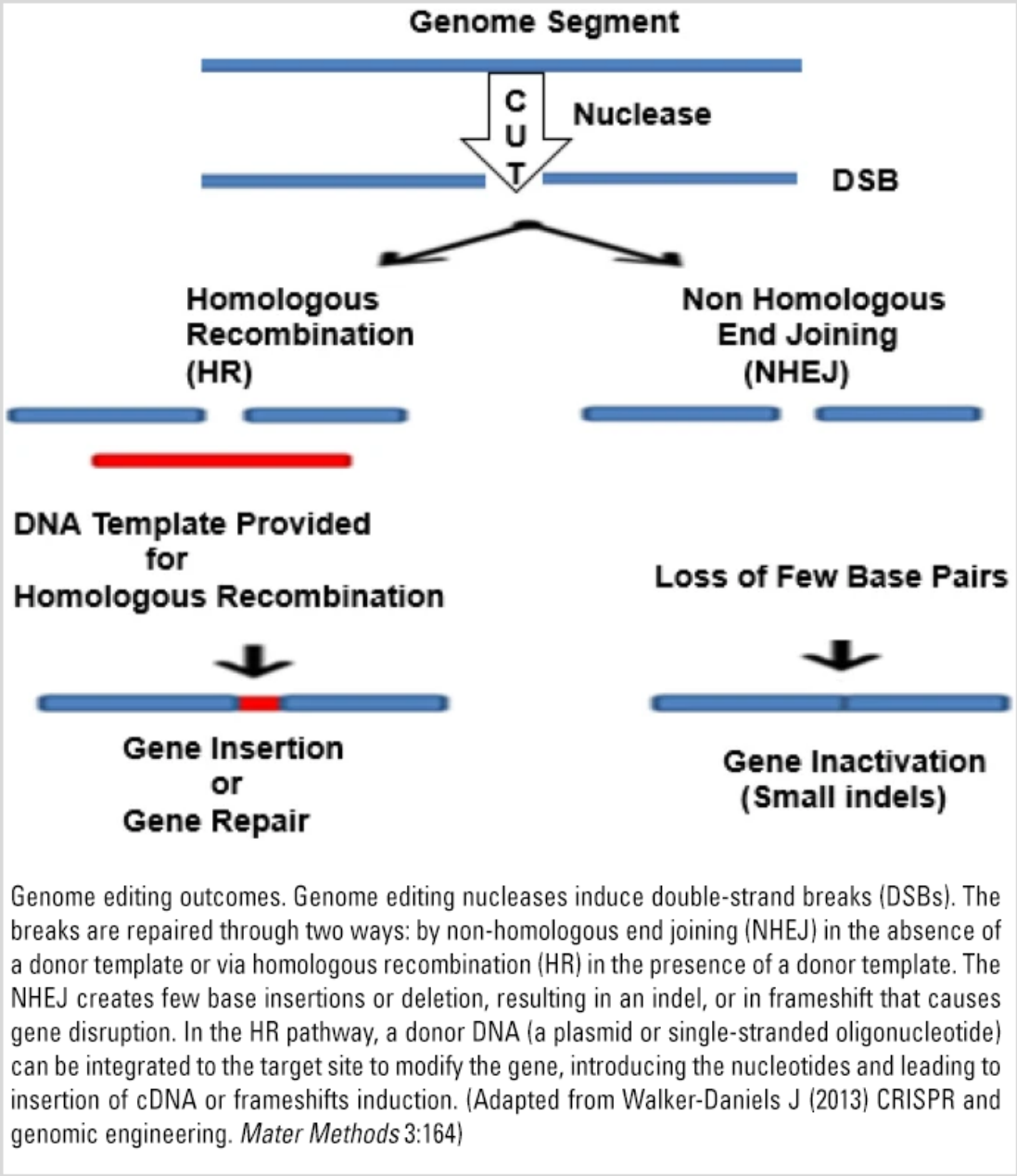
Genome engineering, genome editing, and gene editing are terms that are often used interchangeably; but have distinctions. They can also be referred to as New Plant-Breeding Technologies (NPBT) or precision biotechnologies. According to Robb et al. genome engineering is a process, or field[1,] where the sequence(s) of DNA are designed and modified.[2] Genome editing and gene editing are both techniques used *for* genome engineering that incorporate site-specific modifications into genomic DNA using DNA repair mechanisms.[1,2] Gene editing can be distinguished from genome editing in that it typically focuses only on one gene.[1] Whereas genome editing refers to the targeted changes to non-gene regions in the hopes of inserting new genes or to modify gene-regulatory regions in order to manipulate the functions of existing genes.[2] (See Figure 1) Genome editing has also been compared to other breeding methodologies (e.g. conventional breeding), where the distinctions can be important, particularly for risk assessments and regulatory decision-making (See Figure 2).

Genome editing is not a singular technology or technique; it refers most often to a set of techniques that enable the manipulation of a genome with greater precision than previous iterations of genetic engineering.[6] These tools can include but are not limited to: Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR/Cas9), Transcription Activator-Like Effector Nucleases (TALEN), Zinc-Finger Nucleases (ZNF), and Oligonucleotide Directed Mutagenesis (ODM). They are designed to insert, delete, or alter either one or more DNA nucleotides.[7] Table 1 describes the three main types of genome editing which forms the basis for how many of the country's governance systems described within this discussion documents are based. This is not meant to be a comprehensive list; as genome editing is a rapidly evolving set of technologies. See Jansing et al. for a comprehensive description of genome editing in agriculture.[8]

As discussed throughout this document, many countries in the LAC region have established genome editing specific governance systems while others have not specifically implemented genome editing specific governance systems and appear to include them in their current biosafety frameworks (See: Figure 3). While much of the LAC region appears to be coalescing around a similar interpretation of how genome editing will be governed, it is not yet clear if or how international treaties governing

i Throughout this discussion document, genetically modified organism (GMO) and living modified organism (LMO) will be used interchangeably to accommodate varying regulations and international treaties which use both terms.

these tools (e.g., Cartagena Protocol on Biosafety to the Convention on Biological Diversity) will ultimately decide. This discussion document is a starting point at assessing the landscape of genome editing oversight in LAC, and it provides a broad overview of the state of GMO crops and gene edited crops governance in nine selected countries (Argentina, Bolivia, Brazil, Colombia, Honduras, Mexico, Paraguay, Peru, and Uruguay).



Genome editing outcomes. Genome editing nucleases induce double-strand breaks (DSBs). The breaks are repaired through two ways: by non-homologous end joining (NHEJ) in the absence of a donor template or via homologous recombination (HR) in the presence of a donor template. The NHEJ creates few base insertions or deletion, resulting in an indel, or in frameshift that causes gene disruption. In the HR pathway, a donor DNA (a plasmid or single-stranded oligonucleotide) can be integrated to the target site to modify the gene, introducing the nucleotides and leading to insertion of cDNA or frameshifts induction. (Adapted from Walker-Daniels J (2013) CRISPR and genomic engineering. *Mater Methods* 3:164)

Figure 1. Genome editing outcomes. (Khalil 2020)

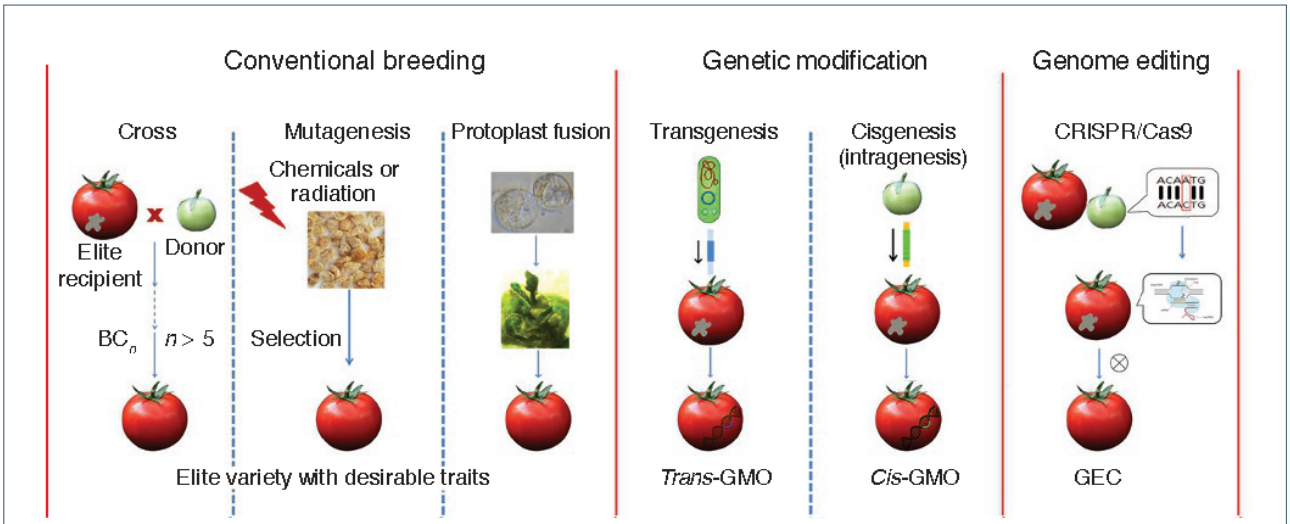


Figure Description: Comparison of three breeding methodologies. Conventional breeding mainly includes sexual crosses, mutagenesis and tissue culture–based techniques. Crosses rely on intra- or interspecific hybridization between a donor and an elite recipient line. The progeny of the cross are selected for the desired characteristic. To remove unwanted traits (shown as a star on the tomato) inherited from the donor plant, the best line of the progeny is obtained by backcrossing with the elite recipient line. Mutagenesis with chemicals or radiation is the process of exposing seeds to mutagens to generate mutants with desirable traits. Protoplast fusion, also called somatic fusion, is a technique where cells from two related species (or two different varieties of the same species) are induced to fuse, to form a new hybrid plant that ideally has characteristics from both parents. Transgenesis is the genetic modification of a recipient line with genes from other species that are sexually incompatible with the recipient plant. Cisgenesis (sometimes called intragenesis) is the genetic modification of a recipient plant transformed with a natural gene for a crossable plant. In genome editing, DNA is directly inserted, replaced or removed from a genome using engineered nucleases, colloquially called 'molecular scissors', to effect a desirable trait. BCn, backcross nth generation; GMO, genetically modified organism; GEC, genome-edited crop; ⊠, self-pollination.

Figure 2. Comparison of three breeding methodologies. Reprinted/adapted by permission from Springer Nature: Nature Genetics "A proposed regulatory framework for genome-edited crops," by Sanwen Huang et al., 2016

Genome Editing Type	Description
SDN1 (site-directed nuclease 1)	Involves the unguided repair of a targeted double-strand break (DSB) by the mechanism called nonhomologous end joining. The spontaneous repair of this break can lead to a mutation causing gene silencing, gene knock-out or a change in the activity of a gene.
SDN2 (site-directed nuclease 2)	Involves a template-guided repair of a targeted DSB using a sequence donor, typically short single-stranded DNA. The donor carries one or several small mutations flanked by two sequences matching both ends of the DSB, and is thus recognized as a repair template, allowing the introduction of the mutation(s) at the target site.
SDN3 (site-directed nuclease 3)	Involves a template-guided repair of a targeted DSB using a sequence donor, typically double-stranded DNA containing an entire gene or an even longer genetic element(s). Both ends of the donor are homologous to the DSB ends (and the donor sequence is usually more than 800 bp each), which therefore recognize the donor as a repair template, allowing the introduction of the gene or genetic element(s) at the target site.

Table 1: Three main types of gene editing. Note, SDN2 or SDN3 donor templates can come from the same or different species (cisgenic or transgenic). Adapted from (Friedrichs et al. 2019b, 2019a).

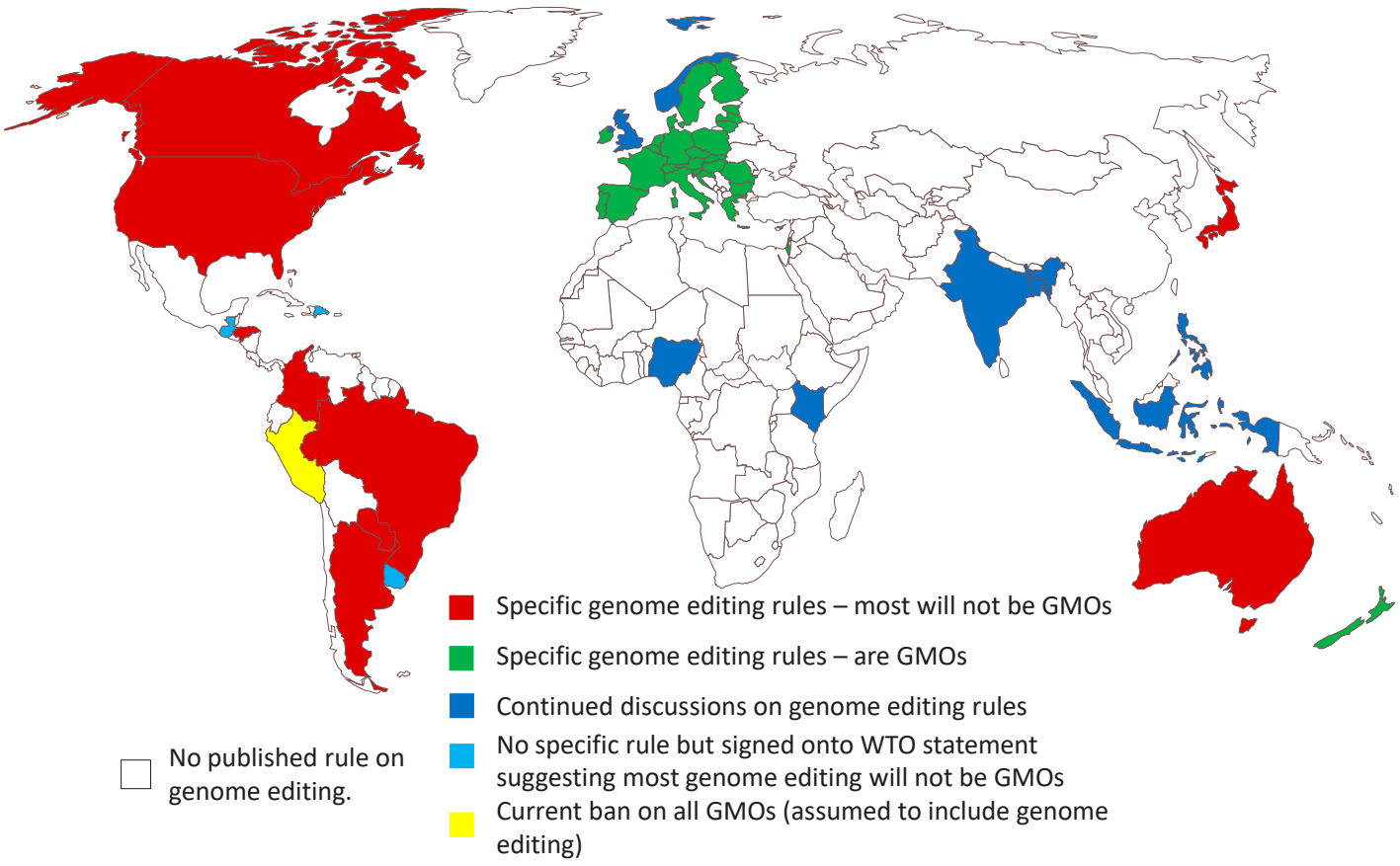


Figure 3. Global Status of genome editing legislation. Updated and adapted from (Schmidt, Belisle, and Frommer 2020). As of February 2021. In countries with genome editing rules; most SDN-1 and SDN-2 will not be GMOs see Table 1.

II. OVERVIEW OF CURRENT GMO/GENOME EDITING LANDSCAPE IN LATIN AMERICA

(Argentina, Bolivia, Brazil, Colombia, Honduras, Mexico, Paraguay, Peru, Uruguay)

A. ARGENTINA

In 2019, Argentina was third in the world in biotech crop area harvested (behind the U.S. and Brazil).[9] Between 94%–100% of its soybean, cotton, and corn traded on world markets come from genetically modified (GM) varieties, and it has approved over 48 GM crops for commercial use.[10] Its regulatory system is also one of the oldest in Latin America, with the key establishment of a multi-institutional commission of experts, the National Advisory Commission for Agricultural Biotechnology (CONABIA, Comision Nacional Asesora de Biotecnologia Agropecuaria), in 1991.[10] CONABIA plays a central role in biosafety assessments and confinement or containment measures for GMO applications, as well as advising more generally on scientific and technical aspects of agricultural biotechnology. Authorities for regulating GMOs come from several government agencies, laws and regulations depicted in Table A1 below. Note, unlike Brazil, which has a specific GMO Biosafety Law, Argentina does not have a specific law to regulate GMOs,[11] but uses general laws for environmental, food, plant, and animal health protection to promulgate regulations (Resolutions) for biotechnology and GMO regulation un-

der those laws.[ii] Argentina is a signatory to the Cartagena Protocol on Biosafety (CPB), and although it has not ratified it, its regulations have been structured to be compatible with the CPB definitions, particular those on LMOs.

Authorities and responsible agencies	Responsibility	Pertinent laws and regulations (only chief instruments are mentioned here)
Ministry of Agroindustry: Secretariat of Foodstuff and Bioeconomy	Decision making (Permits, administrative sanctions) Enacting of main Administrative Regulations	Law 22.520 on the Ministries of the Executive Branch
Biotechnology Directorate	› Coordination of the regulatory framework › CONABIA (Bio safety Assessment) Chair	› Decrees 1940/2008 13/2015 and 32/2016 › Ministerial Resolution 763/11 on the structure of the regulatory system, and several subsidiary regulations
Undersecretariat of agricultural markets	Market assessment for commercial release	Resolution 510/11 for the assessment of impacts on production and commercialization
SENASA	› CTAUOGM (Food Safety Assessment) Chair › Food and plant health police	› Law 27.233 on Animal and Plant Health › Resolution 412/02 on Food and Feed Safety Assessment (domestication of Codex guidelines)
INASE	Seed (e.g. any plant propagative material) police	› Law on Seeds and Phytogenetic creations › Resolution 46/04. GM crops Operators' register

Table A1. Argentina's GMO Authorities, Laws, and Regulations. Adapted from (Whelan and Lema 2019).

Efforts to interpret the GMO regulations for genome editing in plants began relatively early in Argentina compared to the rest of the world.[12] In 2015, the Ministry of Agroindustry issued Resolution 173 (aka 173/15) to interpret Argentina's GMO regulations for genome edited (GED) crops with regard to whether they are GMOs or not under previous resolutions 701/11 and 763/11. This resolution did not alter previous GMO regulations, nor determine certain categories of GED crops as "exempt" from these regulations.[iii] Rather, it set forth the procedure to determine whether a GED crop would be subject to pre-existing GMO regulations according to the key criteria of "novel combination of genetic material."[10]

In 2021, Argentina published further clarification of the "new plant breeding technology" approval process, a definition of "new combination of genetic material" to guide review of NPBTs under

ii This is a similar approach to the U.S. which uses existing food safety, animal and plant health, and environmental protection laws to regulate GMOs.

iii Note this differs from the USDA SECURE rule which exempts SDN-1 and SDN-2 (if gene edit sequence is in same gene pool) right off the bat. Developers can consult with USDA to confirm, but do not have to do so.

CONABIA, and articles to guide what types of information submitted by developers can and cannot be claimed as confidential business information (Resolution 20/2021).

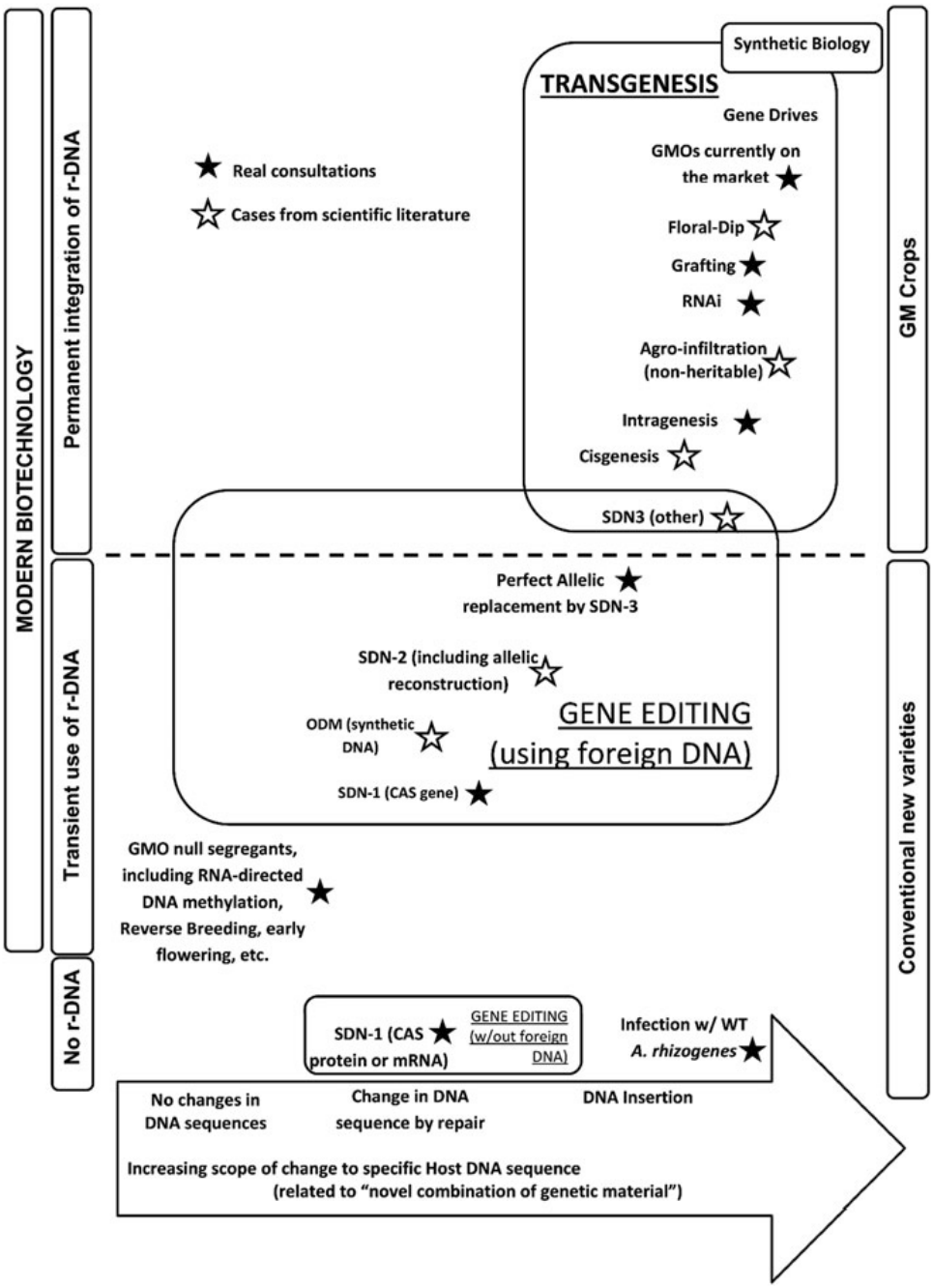


Figure A1. Likely Biotech crop classification in Argentina. Reprinted/adapted by permission from Springer Nature: Springer eBook "Regulation of Genome Editing in Plant Biotechnology: Argentina," by Agustina I. Whelan and Martin A. Lema, 2019

Although each GED crop will be assessed on a case-by-case basis, and Resolution 173/15 does not itself contain a list of methods that determines whether or not a GED crop will be classified as non-GMO,[iv,13] Figure A1 show categories of GED crops that are likely to fall outside of Argentina's GMO regulations (below the dotted line) and those likely to fall within them (above the dotted line) according to regulators who authored the figure at the time. GED crops made by ODM, SDN-1 (homologous repair), and SDN-2 (insertions or deletions that are found in species gene pool already and do not result in novel combinations) are likely to fall outside of the Argentina definitions of GMO, as long as any transgenic or foreign DNA used in the process is removed from the product submitted to the regulatory authorities. However, all of these GEDs must still be submitted to a central point for review, CONABIA, in order to make the determination of whether the GED plant is a GMO or not.

To submit a GED to CONABIA, an applicant must be registered under the National Registry of Operators with GM Plant Organisms (Resolution 46/04) through the National Seeds Institute (INASE). Once a product is submitted to CONABIA, it is reviewed according to the process outlined in Figure A2 as to whether it is GMO and falls under the regulations in Table A1. For this review, the applicant needs to submit the breeding methodology used to develop the crop, information about the new trait, and the genetic changes in the final product at this stage. The consultation is required because the GED is presumed to be GM until CONABIA establishes otherwise.[10] If a transgenic gene construct is used transiently, scientific information must be provided to ensure that integration in the plant genome has not occurred or has been removed through backcrossing or outbreeding (e.g., to show that it is a "null segregant"). Developers of GED crops can consult with CONABIA in design stages

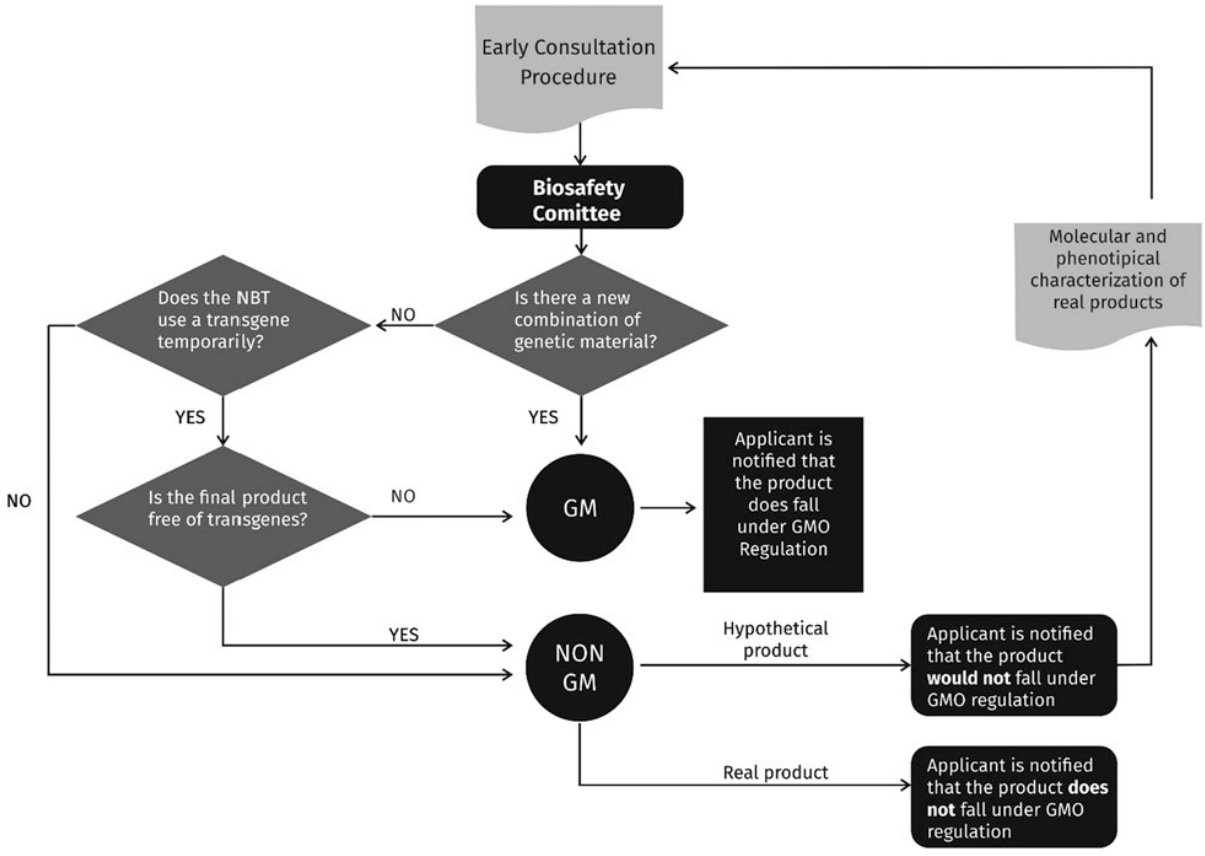


Figure A2. Sixty-day evaluation for GMO status in Argentina. From (Whelan and Lema 2019).

iv This differs from the Brazilian resolution which does contain a non-exhaustive list with examples of techniques that could originate a product considered as non-GMO(Gatica-Arias 2020).

to determine whether a GED crop is likely to be determined as GMO or not, but still must return and submit the molecular biology studies when the GED crop is finally developed to show no integration of "novel combinations of genetic material." A determination of GMO status is to be made within a 60-day time frame. Resolution 173/15 also has special provisions for follow-up measures if the GED crop is determined to be non-GMO but has features that may warrant further evaluation of risk. If risk issues are triggered for "non-GMO" GED crops, these crops can be referred to regulatory agencies that assess conventionally bred varieties for various purposes (seed, food, feed, etc.).[v]

If the GED plant is determined to be a GMO and the applicant wants to bring it outside of the laboratory or greenhouse, they must apply for a field trial permit under Resolution 763/11 which is regulated by the Biotechnology Directorate under the Secretariat of Foodstuff and Bioeconomy within the Ministry of Agroindustry. CONABIA provides the technical safety assessment and evaluation, which the Ministry uses for its decision. Authorization for full commercial release of GED crops, if it is determined to be a GMO, is also regulated by Resolution 763/11 and undergoes three main assessments: 1) a biosafety assessment by CONABIA; 2) a food safety assessment performed by the National Agrifood Health and Quality Service's (SENASA) Food Safety Assessment Chair (CTAUOGM) according to Resolution 412/02; and, 3) a production and commercial impacts assessment under the Undersecretariat of Agricultural Markets (SSMA) of the Ministry of Agroindustry and Resolution 510/11.[vi] All three assessments are taken under advisement by the Secretary of Foodstuffs and Bioeconomy for a final decision on approval. Other regulations also exist in Argentina pertaining to seed and biomass production only or non-cultivation importation for food, feed and processing.[10]

There is no mandatory labelling of GM food, feed, or other GM products in Argentina, and thus there would be no labeling of GED food, feed, or products.[10] However, there is also no allowance in the GM regulations for low-level, adventitious presence of non-approved GMO varieties in food, feed, products, or seed. Likewise, if a GED were determined to be an unapproved GMO, there would also be a zero-tolerance for its presence in Argentina.

The exact number of GED crops reviewed and/or approved for cultivation by Argentina at this time may not be known, as some authors note that the public does not have access to a database of approved GED crops and these regulatory decisions are not communicated to the public.[13–15] However, in the literature, there are reports of at least 25 applications since 2015[13,16] for annual crops, ornamental plants, and fruit trees, including traits from herbicide resistance to consumer or industry value-added traits.[12,16] Reported public-sector research on GED crops includes non-browning potatoes and increased alfalfa productivity.[13] Whelan et al. (2020) also report that three New Plant-Breeding Technology (NPBT) crops have been classified as GMOs in Argentina's regulatory system since 2015, and over 22 have been classified as non-GMO. These are likely to include several GED crops. However, they do not indicate whether these crops are now on the market or commercialized. In comparison to 1st generation GM crops, GED crops classified as non-GMO in the Argentinian regulatory system are more likely to be from local companies and public research institutes—that is, 8% of 1st generation GM crops were from local companies and public research institutes in Argentina in comparison to 59% of NPBT or GED crops.[16] There is also a higher diversity in terms of traits and biological kingdoms in GED and NPBT crops than in 1st generation GM crops in Argentina.[16]

v For example, the National Commission on Seeds (CONCASE) can assess for sanitary issues like harmful metabolites or pest susceptibility and refer to SENSA for supplementary analysis.

vi Note, there is no such formal regulatory assessment for these trade and socioeconomic impacts in the United States.

B. BOLIVIA

Bolivia was ranked 10th globally in total hectares of biotech crops planted in 2019, with 1.4 million hectares of soybean planted.[9] According to the U.S. Department of Agriculture (USDA) Foreign Agricultural Service, the Government of Bolivia approved two new genetically engineered soybean products in 2019 and was considering the approval for corn and cotton.[17] Prior to that, the only GMO seed approved for cultivation in Bolivia was a glyphosate-resistant soybean.[18] As of 2020, there is no evidence that any gene-edited products have been submitted for evaluation or approved for use.

Bolivia ratified the Cartagena Protocol on Biosafety (CPB) in 2002. Bolivia has implemented a host of laws, regulations, and Presidential decrees that have governed the importation, use, and trade of GMOs, which have shifted over time:

› **Article 255 of the Constitution (2009) (CPE),** which prohibits all forms of production, import and marketing of GMOs.

› **Administrative Resolution No. 135/05 VRNMA,** which protects maize from any possibility of transgenic contamination.

› **Executive Decree No. 181 (Article 80),** which prohibits the purchasing of GMO foods in government procurement and school feeding programs.

› **The Law of the Rights of Mother Earth (Law No. 071),** which establishes "the right to the conservation and protection of the diversity that makes up Mother Earth, without being genetically altered or modified in its structure in an artificial way…"

› **Law No. 144, the Law of Communal Productive Agricultural Revolution** *(Ley de Revolución Productiva Comunitaria Agropecuaria)*, which protects species for which Bolivia is a center of origin or center of diversity—including maize, cotton, and many other crops—from any possibility of transgenic contamination.

› **Article 24 of the Law of Mother Earth and Integrated Development for "Living Well"** *(Ley Marco de la Madre Tierra y Desarrollo Integral*, Law No. 300) outlines the state's obligation to take action toward the gradual elimination of GMO crops from the country.

As the government and political parties of Bolivia has changed hands over the years, the governmental views towards GMOs have also shifted. For example, Article 255 in 2009 which had banned GMOs has evolved into Supreme Decree No. 24676 described below which has enabled the importation and use of GMOs. These shifts in political power and agendas towards GMOs will be important to track over time as genome editing becomes more prevalent and their governance systems emerge in Bolivia.

The overarching GMO regulations and assessments in Bolivia are guided by Supreme Decree No. 24676, which encompass the regulations for Decision 391 that brings Bolivia into compliance with the CPB.[18] It establishes an application and review procedure for the development, importation, planting, and commercial use of LMOs. The review process consists of three risk evaluations: 1) the possible negative impacts on human health, the environment and biological diversity arising from the activity carried out with the GMO; 2) the feasibility of managing the risks based on the management measures proposed by the applicant; and 3) the classification of the GMO into one of two categories:

› **Group 1:** A GMO shall be classified in this group and considered of low risk according to the following criteria: (i) there is no likelihood that the receiving or parent organism could cause disease in human beings, animals, or plants; (ii) the nature of the vector and of the insert is such that it

does not supply the GMO with a genotype that is likely to cause disease in human beings, animals, or plants, or that is likely to have adverse impacts on the environment; (iii) it is not likely that the GMO will cause disease in human beings, animals or plants, and it is highly unlikely that it will have adverse effects on the environment.

› **Group 2:** A GMO shall be classified in this group and considered of high risk when it does not meet the requirements established in Group 1, that is, the receiving or parent organism, the nature of the vector and the insert as well as the GMO or one of them, causes disease in human beings, animals and plants, and has adverse impacts on the environment.[18]

The regulation lays out a series of definitions (biotechnology, genetic engineering, genetically modified organism) that could impact how gene edited products are evaluated under the law:

› **Biotechnology:** Any technological application that uses biological systems and living organisms or their by-products for the creation or modification of products or processes for specific uses.

› **Genetic engineering:** Process whereby the gene of one organism is transferred to another through the manipulation of the genetic information (genes).

› **Genetically modified organism (GMO):** Any organism whose genetic material has been altered by any technique of genetic engineering.[18]

The specificity of what constitutes genetic engineering—notably the transfer of a gene from one organism to another—and the subsequent requirement that a GMO is "any organism whose genetic material has been altered by any technique of genetic engineering," will need to be evaluated against the tools of genome editing and the resulting genetic changes. Clarifying and potentially aligning these varying definitions will be important in determining whether genome editing applications will be classified as a GMO and subject to the various GMO laws in Bolivia and amongst its international trading partners.

C. BRAZIL

Brazil is currently second in the world in biotech crop area harvested, behind only the U.S.,[9] with over 100 events (particular genetic trait-transformation event combinations) in GM crops approved.[19] In 2019, biotechnology crop adoption in Brazil constituted 94% of soybeans, 95% of cotton, 88% of first-crop corn, and 78% of second-crop corn.[19]

Whereas Argentina and many other countries in the world (including the U.S.) interpret existing laws to promulgate regulations on GMOs, Brazil has a specific law dealing with GMOs, Biosafety Law 11, 105/2005. This law outlines the regulatory framework for agricultural biotechnology in Brazil. Article 1 of the law:

> "Establishes the security standards and inspection mechanisms on the building, cultivation, production, handling, transport, transfer, import, export, storage, research, commercialization, consumption, release into the environment and disposal of genetically modified organisms—*GMOs and their derivatives*, based on the guiding principles of the promotion of scientific advances in the areas of biosafety and biotechnology, protection of human, animal, and plant life and health, and observance of the precautionary principle for the protection of the environment."

Some key definitions in Article 3 of the law include "GMO: organism whose genetic material—DNA/RNA—has been modified by any genetic engineering technique," and "genetic engineering: the ac-

tivity of the production or handling of recombinant DNA/RNA molecules." The law also applies to products obtained from GMOs, such as food or feed, as they are "GMO derivatives."

Article 3 also states that "§1 The GMO category shall not include that which results from techniques which imply the direct introduction, into an organism, of hereditary material, as long as *they do not involve the use of recombinant DNA/RNA molecules or GMOs*," and "§2 The GMO derivative category shall not include a pure substance, chemically defined, obtained by means of biological processes and which does not contain a GMO, heterologous protein, or recombinant DNA." The presence of rDNA molecules is thus an important part of the regulatory authority under Law 11,105/2005. Under Article 4, the law also does not apply to the following techniques as long as they do not involve the use of a GMO as a receiver or donor: "mutagenesis, formation and use of somatic cells of an animal hybridoma, cellular fusion, and auto cloning of nonpathogenic organisms processed in a natural manner."

In 2018, Normative Resolution No. 16 (16/2018) was published to outline the evaluation process for whether a product developed using new breeding technologies (NBTs), called Innovative Precision Breeding Techniques (TIMP, Técnicas Inovadoras de Melhoramento de Precisão, such as genome editing, would be considered GMO under the scope of the Biosafety Law 11,105/2005. Like Argentina's resolution 173/2015, Brazil's RN 16/2018 establishes the requirements for a consultation on whether a product is exempt from the GMO regulatory framework or not. However, in contrast to Argentina's Resolution 173/15, Brazil's Resolution 16/2018's includes a non-exhaustive listing of examples of techniques that would likely lead to a product not being considered a GMO in its Annex I.

The § 3rd Article 1 of Normative 16/2018 establishes the characteristics that would be reviewed by

Paragraph 3. The products referred to in the main section of this article show at least one of the following characteristics:
I – Product with proved lack of recombinant DNA/RNA, obtained with a technique using parental GMO;
II – Product obtained through a technique using DNA/RNA which will not multiply in a living cell;
III – Product obtained by a technique which introduces site-directed mutations producing genic function gain or loss, but proved absence of recombinant DNA/RNA in the product;
IV – Product obtained by a technique in which there is temporary or permanent expression of recombinant DNA/RNA molecules, but no presence or introgression of these molecules in the product; and
V – Product which uses techniques employing DNA/RNA molecules that do not modify permanently a plant's genome when in contact, or systemically or non-systemically absorbed by it.

Table B1. NPBT in crops which require CNTBIO review under RN 16/2018. Adapted from (Normative Resolution No. 16, of January 15, 2018).

CNTBio to determine the regulatory status for the product obtained using TIMP (Table B1). While Argentina's 173/2015 Resolution have the definition of a LMO from the CPB (Cartagena Protocol on Biosafety) CPB and uses the definition of GMO and derivatives from the national Biosafety Law 11,105/2005. However, Brazil's resolution is likely to result in similar decisions as to whether GED

crops are non-GMO.[vii] [10,13,15] Table B1 indicates that "proving absence of recombinant DNA/RNA in the final product" is a key determinant of a GED crop exemption from Brazil's GMO regulations.

A specific, but non-exhaustive listing of techniques that could not be considered as GMO if used for crop biotechnology is included under RN 16/2018 Annex I (Table B2). Methods include site directed mutagenesis and oligonucleotide directed mutagenesis. However, RN 16/2018 includes the caveat that examples of TIMP currently presented as examples in Annex 1 are limited and may be extended in the future to other forthcoming techniques.

vii Argentina and Brazil may differ with decisions about cisgenesis (Brazil has not listed it yet in Annex I) and Grafting (Brazil exempts it whereas Argentina is likely not to do so) according to Gatica-Arias (2020) Table 2.

TECHNIQUE	SUMMARY
1. Early flowering	1.1 Silencing and / or super-expression of genes related to flowering by inserting genetic modification into the genome and subsequent separation or through transient expression by viral vector.
2. Seed Producing Technology	2.1 Inserting fertility-restoring genetic modification in naturally male- sterile lines in order to multiply these lines maintaining the male-sterile condition but not transmitting the genetic modification to descendants.
3. Reverse breeding	3.1 Inhibiting meiotic recombination in heterozygous plants selected for the trait of interest in order to produce homozygous parental lines.
4. RNA-dependent DNA methylation	4.1 Methylation driven by RNA interference ("RNAi") in RNAi homologous promoter regions in order to inhibit target gene transcription in live beings.
5. Site-Directed Mutagenesis	5.1. Protein or riboprotein complexes capable of causing site directed mutagenesis in microorganisms, plants, animals, and human cells.
6. Oligonucleotide Directed Mutagenesis	6.1 A synthesized oligonucleotide containing one or a few nucleotide alterations complementary to the targeted sequence, on being introduced into the cell, may cause substitution, insertion or deletion in the target sequence through the cellular repair mechanism microorganisms, plants, animals, and human cells).
7. Agroinfiltration / agroinfection	7.1 Foliage (or other somatic tissue) infiltrated with Agrobacterium sp. or gene constructs containing the gene of interest to obtain a temporary expression at high levels located in the infiltrated area or with viral vector for systemic expression without the modification being transmitted to subsequent generations
8. Topical/systemic use RNAi	8.1 Use of double-stranded RNA ("dsRNA") with targeted-gene homologous sequence specifically silencing this gene or genes. Engineered dsRNA molecules may be introduced/absorbed into the cell from the environment.
9. Viral vector	9.1 Inoculation of live beings with recombinant viruses (DNA or RNA) expressing the genetic modification and amplification of the gene of interest through viral replication mechanisms without host genome modification.

Table B2. New Plant Breeding Innovations in Annex 1 of Brazil's rn 16/2018. Adapted from (Normative Resolution No. 16, of January 15, 2018).

Under RN 16/2018 Article 2, inquiries for whether a GED is subject to GMO regulations should be submitted to CNTBio. CTNBio then interprets RN 16/2018 to regulate NPBTs as GMO or non-GMO on a case-by-case basis. Annex II of RN 16/2018 provides a list of technical information that should be submitted for CNTBio review to determine GMO regulatory status. These include the molecular map of the constructs used, the genes manipulated and their function, the purpose or use of the end product, molecular data of parental and progeny showing the absence of rDNA in the progeny, product approvals in other countries, and evidence of unintentional effects (off-target mutations) in the end product.[viii] CNTBio has 90 to 120 days to make a non-GMO determination.[15]

As mentioned, CTNBio will generally exempt GED crops from biosafety regulation when there is no insertion of transgenes or rDNA.[19] Thus, genome editing using SDN-1 (homologous repair) or SDN-2 (removing the final presence of transgenes) are likely to be exempt, although SDN-3 (insertion of transgenes due to genome editing) would not be.[13] For the latter non-exempt category, the full risk assessment and management of "GMOs" would be applied to the GED crop. Like most other regulatory systems in the world, Brazil's regulatory system is considered a hybrid of *product and process-based regulation*—although evaluation is focused on the final biotech crop or derivative-product, the use of genetic engineering is the trigger for the consultation process and decision-making by CTNBio.[19]

As of early 2020, there were reports of at least seven application for new breeding technologies in plants, microorganisms, and animals that have been reviewed by CNTBio.[13,19] One of these was a GED plant, waxy variety of maize, which was determined not to be a GMO according to RN 16/2018.[13,19] Public and private sector research and development on GED crops is occurring in Brazil. For example, U.S. based CORTEVA AgroSciences and Brazil's Agricultural Research Corporation (EMBRAPA) signed a partnership agreement for research using CRISPR that allows EMBRAPA to use the technology in plants for agricultural use.[19] The first research project underway involves the development of drought tolerant and nematode resistant soybean varieties using CRISPR.

D. COLOMBIA

In 2019 Colombia had planted approximately 100,000 hectares of GMO maize and cotton and was ranked 18th in the world in total area of biotech crops planted.[9] Colombia ratified the Cartagena Protocol in 2003. Law 70 ratified the Cartagena Protocol and subjects Colombia to its requirements which are embedded within Decree 4525 and its evaluation process of living modified organisms (LMOs) which are done on a case-by-case basis.

Colombia, like other countries, lays out a series of definitions which guide its biotechnology governance regimes. Colombia has an additional definition for genetically modified organisms (GMOs) that goes beyond the definition for LMOs as described in the CPB by including terms like "developments" and "advances" that could impact how gene edited products are evaluated under the law.

Decree 4525, issued in 2005, established a set of National Technical Biosecurity Committees responsible for the evaluation of biotechnology products, including the associated risk assessments. These include the Ministry of the Environment, Housing, and Territorial Development (MEHTD), the Ministry of Health and Social Protection (MHSP), and the Ministry of Agriculture and Rural Development (MARD). These recommendations are submitted and managed through the Colombian Agricultural Institute (ICA), Colciencias (Colombian Science and Technology Agency), and the National Institute for the Surveillance of Food and Medicines (INVIMA), who ultimately make the final decision. There are separate requirements and review procedures for contained research activities as opposed to open field release or approval of food or feed. See Figures C1-C3 for approval process.

viii Note: in the U.S. USDA under SECURE has decided not to require review of potential off-target mutations.

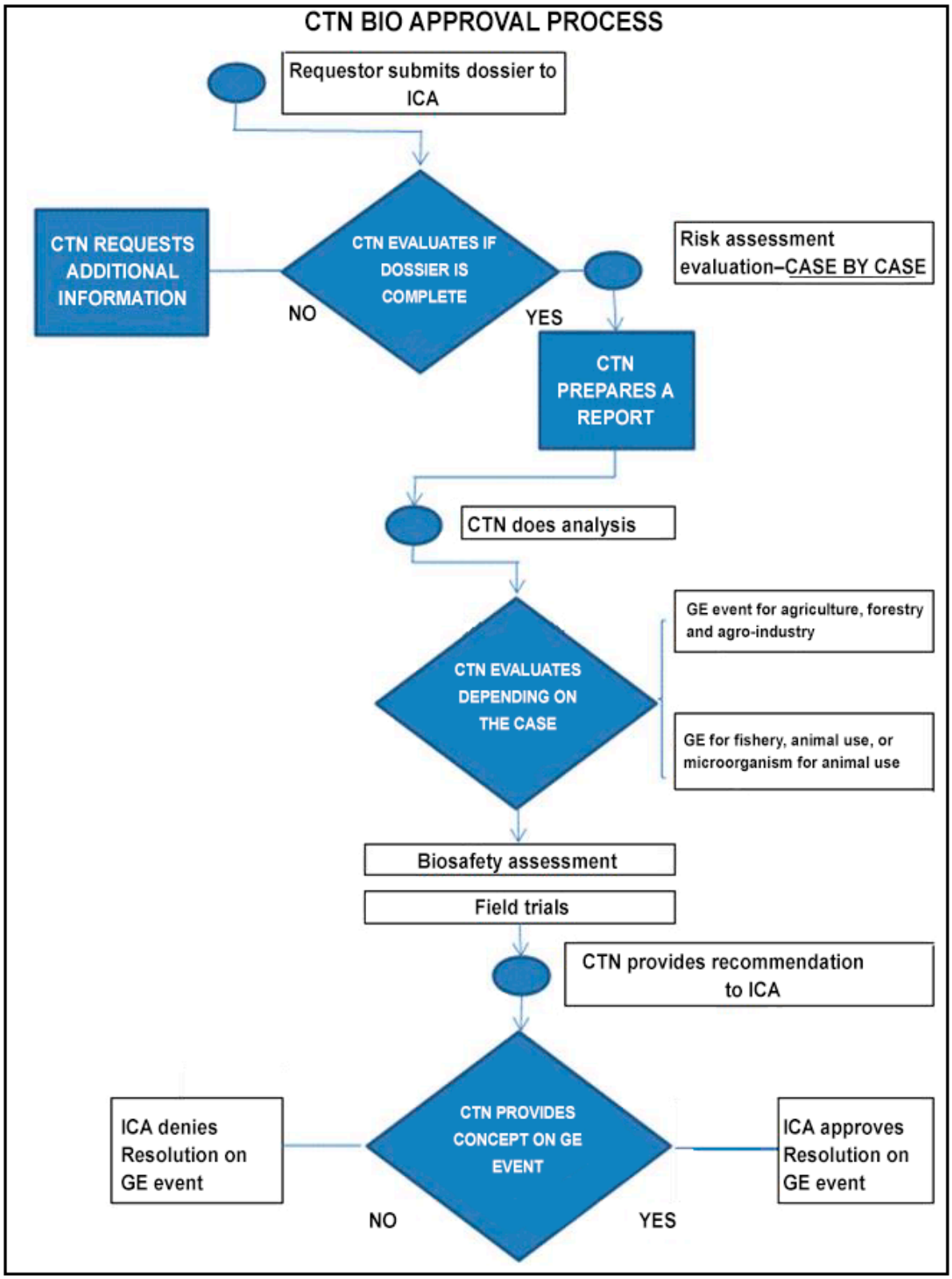


Figure C1. Colombian Science and Technology Agency approval process for non-food related products. From (United States Department of Agriculture Foreign Agricultural Service 2020).

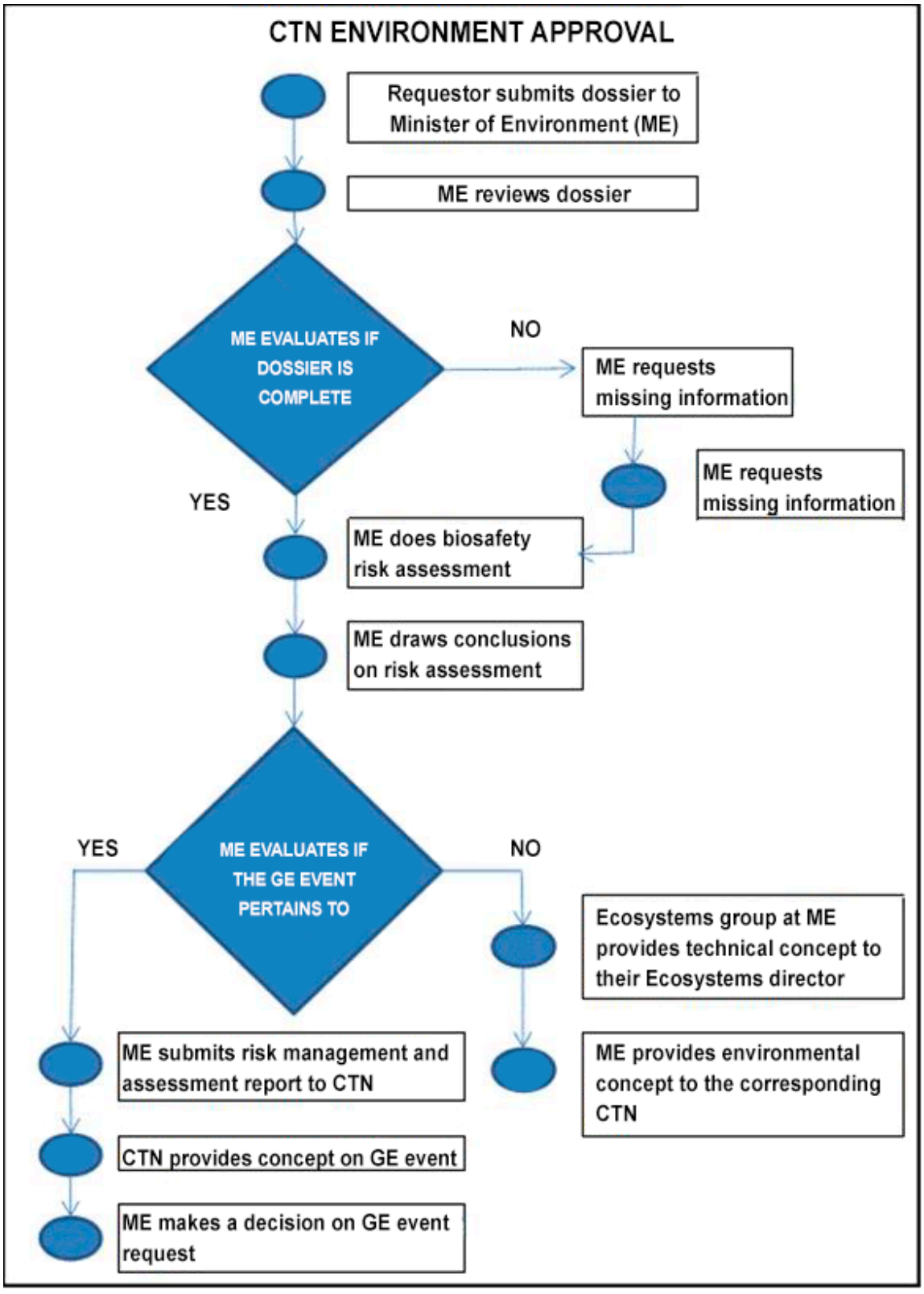


Figure C2. Colombian Science and Technology Agency approval process for environmental release. From (United States Department of Agriculture Foreign Agricultural Service 2020).

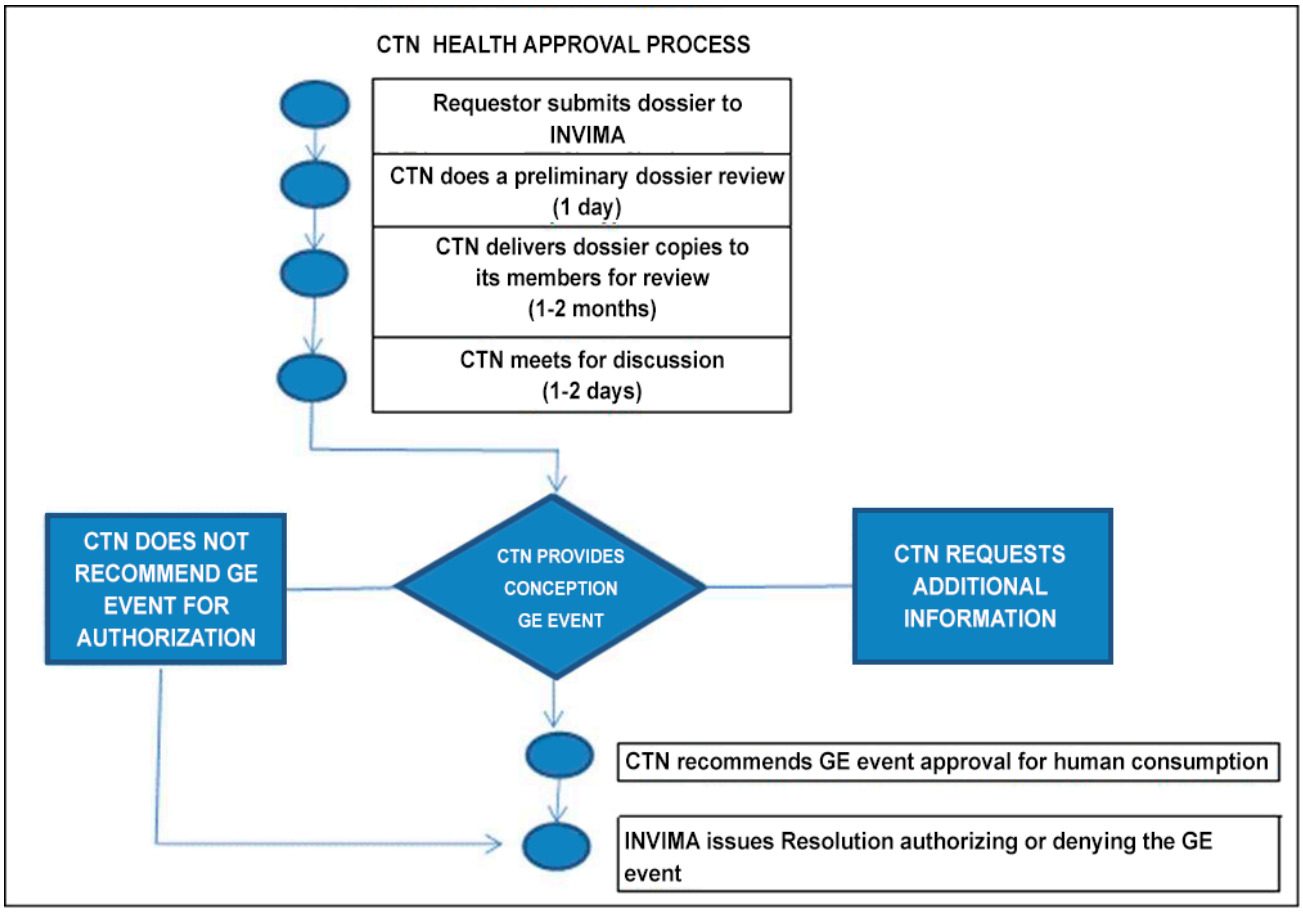


Figure C3. Colombian Science and Technology Agency approval process for human health impacts. From (United States Department of Agriculture Foreign Agricultural Service 2020).

In 2018, resolution no. 29299/2018 established a procedure to determine whether applications developed using genome editing techniques are LMOs or not.13 This case-by-case assessment of gene edited products focuses on whether the final product contains foreign DNA sequences.[13] Applicants must provide the taxonomic classification of the species, breeding methodology, genetic maps of the genetic constructs used in the breeding process, including the protein and RNA sequences used, a description of the phenotype and its uses, the molecular characterization of the genetic changes in the end product compared to the original, and finally, prove the absence of foreign genetic material.[13] The application is reviewed for up to 60 days to determine whether the product meets the definition of a Living Modified Organism. If the product meets this definition it will have to go through the existing regulatory framework for LMOs under Decree 4525, including a risk assessment and field trials. If the product is determined to not be an LMO it will be treated under existing conventional crop regulations. Resolution 29299/2018 appears to follow Argentina's which would exclude many products of genome editing; particularly those developed via SDN-1, SDN-2, and ODM techniques.[13,20,21]

In 2020, there were two genome editing applications under review.[22] A waxy corn modified for altered starch composition and a phosphorus altered rice, with decreased phosphorus in the grains, but increased levels in the leaves.[22] Colombian researchers are also studying whether CRISPR can be used to modify cassava for resistance against *Xanthomonas axonopodis* and whether varieties of cacao can be developed with reduced cadmium capacity.[13] Although there is no evidence that these applications have been submitted for review against resolution 29299/2018.

E. HONDURAS

In 2019, Honduras was ranked 20th in relation to hectares of biotech crops; about 100,000 hectares of maize.[9] Honduras ratified the CPB in 2008 and it went into force the following year. Honduras has been regulating products of biotechnology since 1998 via the "Biosecurity Regulation with Emphasis on Transgenic Plants."[23] While the law has been implemented since 1998, it wasn't officially a regulation until 2018, when the "Guide of Processes and Procedures of the Regulatory System for Genetically Modified Organisms" was published in the official Gazette.[23] The National Service of Food Safety, Plant, and Animal Health (SENASA) is the regulatory authority responsible for the evaluation of GMOs to the National Committee on Biotechnology and Biosecurity. The regulation captures food, feed, seed, and the environmental implications of the application and covers the import request, field testing, and commercialization. GMO applications are evaluated on a case-by-case basis. Article 2 of the Honduran law uses a very specific definition of genetic modification techniques, which is a requirement for an application to be considered a GMO; "techniques that involve the insertion of DNA from outside the cell."

In 2019 SENASA approved an updated procedure to evaluate gene edited products against the 1998 biotechnology regulation. Based upon the following statement and definitions in the updated procedure, it appears that some genome editing products will not be considered GMOs.

> "That the advancement of science and technology allows the development of new varieties of plants and organism through new techniques known as precision improvement techniques, genome editing, plant improvement innovation or modern genetic improvement techniques without this resulting in a living modified organism. **The latter is of great importance in the application of Honduran regulations, since these are genetic improvement procedures that use the precise knowledge of the relationship between genotype and phenotype and the tools of molecular biology, to develop an organism that in most cases is equivalent between or indistinguishable from which they can be developed using traditional improvement techniques.**"[24]

› **LMO Definition under genome editing rule**: "The definition of Living Modified Organism will be that typified in the Cartagena Protocol on Biotechnology Safety, understanding by new combination of genetic material, a stable insertion into the genome of one or more genes or DNA sequences that encode proteins, RNA, double-stranded DNA or regulatory sequences, *which could not be obtained by conventional improvement, are not found in nature, or are not the result of spontaneous or induced mutations*."[24]

› **Definition of genome editing**: "Those procedures of genetic improvement that use the precise knowledge of the relationship between genotype and phenotype and *the tools of molecular biology* that allow the development of an organism that in most cases is *equivalent or indistinguishable to that which can be developed using traditional techniques of genetic improvement*."[24]

The review process requires SENASA to make a determination of the GMO status of gene edited crops within 45 days of the application being submitted.[24] Article 5 of the updated procedures sets forth the National Committee on Biosafety and Agricultural Biotechnology to work with other countries in the region to harmonize its regulations to "preserve interregional trade in search of products being considered in a similar way in the region."[24]

Honduras' interpretation of genome editing application and their apparent exclusion from being ruled an LMO appears in line with other countries in the region (e.g., Brazil, Paraguay, Uruguay, and

Argentina). This coalescing around a similar viewpoint will be important to monitor as discussions of genome editing within the CPB develops.

F. MEXICO

In 2019, Mexico was ranked 16th in terms of total hectares of biotech crops planted, with approximately 200,000 hectares of cotton.[9] However, Mexico has not approved any new GMOs since May 2018 and in 2019 rejected permits for future plantings of GMO cotton which had been previously approved.[25]

In December 2020, the Mexican President issued a decree banning all imports and approvals of GMO corn. Article six of the Decree states:

> "With the purpose of contributing to food security and sovereignty and as a special measure of protection to native corn, the milpa, the biocultural wealth, the peasant communities, the gastronomic heritage and the health of Mexican women and men, the biosafety authorities, within the scope of their competence, in accordance with the applicable regulations, will revoke and refrain from granting permits for the release into the environment of genetically modified corn seeds.
>
> Likewise, the biosafety authorities, within the scope of their competence, in accordance with the applicable regulations and based on criteria of sufficiency in the supply of corn grain without glyphosate, will revoke and refrain from granting authorizations for the use of genetically modified corn grain in the diet of Mexican women and men, until it is fully replaced on a date that may not be later than January 31, 2024, in accordance with the country's food self-sufficiency policies and with the established transition period in the first article of this Decree."[26]

It is not clear how recent changes in Mexico's regulatory stance towards GMOs and its membership in the United States-Canada-Mexico Agreement (USMCA) will be impacted. Prior to this decree, Mexico was one of the world's largest importers of GMO corn and soy.[25]

Mexico ratified the CPB in 2002 and it went into effect in 2003. Agricultural biotechnology is regulated under Mexico's Biosafety Law,[27] which was implemented in 2005. It regulates the research, production, and marketing of biotechnology related products. The Secretariat of Agriculture and Rural Development (SADER) is the responsible agency for GMO animals, plants, and microorganisms. Under the Biosafety Law SADER evaluates on a case-by-case basis the potential risks to animal, plant, aquatic health, as well as impact to environmental and biological diversity. Based upon the risk assessment requirements and evaluations described in the Biosafety Law, SADER determines whether to issue permits for the introduction of GMOs including field trials and commercial use, amongst other activities. These permits must be renewed annually. Subsequent processes and agreements factor into the risk assessments and final determinations of approval, including the Agreement to Determine the Centers of Origin and Centers of Genetic Diversity of Corn, which restricts the use and storage of GMO corn seeds, the Notification Process for the Confined Use of GMO organisms, and a labeling standard for GMO seeds.

The 2005 Biosafety Law was updated and clarified in 2018, when the requirements for the risk assessment of experimental and pilot stage cultivation of GMOs was issued.[25,28]

Mexico has not yet determined whether genome editing will be evaluated differently or treated the same as GMOs under its Biosafety Law. It will be important to monitor these discussions and any official statements coming from the Secretariat of Agriculture and Rural Development on these issues.

G. PARAGUAY

Like other LAC countries, agriculture is a critical economic sector in Paraguay. Key crops are soybean, cassava maize, wheat, sugar cane, and cotton; and Paraguay is the world's 4th largest exporter of soybean behind Brazil, the U.S., and Argentina.[29,30] Paraguay is also the 6th largest producer of GE crops (behind Brazil, Argentina, U.S., Canada, and India).[9] At least 38 events have been approved and include cotton, maize, and soybean; with 94% of soybean planted in GM varieties, 36% of maize, and 56% of cotton.[31] However, to date, locally developed GM crops have not been submitted for approval.[31]

Biotech crop regulation in Paraguay stems back to 1997 through its use of pre-existing legal instruments, including laws on Seed and Crop Protection (Nbr 385/94); Evaluation of Environmental Impact Law (Nr. 293/93); Phytosanitary Protection (Law Nr. 123/91); Wildlife (Law Nr. 96/92); Protected Wild Areas (Law Nr. 352/94); Forestry (Law 422/733); Defense of Consumer and User (Law Nr. 1.334/98); and the Sanitary Code (Law Nr. 836/80).[32] The first GM crop was approved in 2004, a variety of Roundup Ready soybean.

A key point in the development of a more coordinated regulatory framework for GM crops came in 2012, when the Ministry of Agriculture and Livestock (MAG) established the National Agricultural and Forestry Biosafety Commission (CONBIO)[ix] under Article 1 of Decree 9699.[31,33] This paved the way for further GM crop approvals in Paraguay. CONBIO provides technical analysis and advises on the introduction, field trials, and environmental release of biotech plants. The commission acts as an advisory body and includes representatives of the Ministry of Health, the Ministry of Agriculture and Livestock, and the Ministry of Environment, as well as representatives of scientific institutions, academe, and the farming sector.[31,33–35]

In 2019, MAG promulgated resolutions 1030 and 1071 to differentiate regulatory treatment for commercial release of novel GM crops that have already been approved in other countries.[31,36] These resolutions allowed for the use of decision documents from third-party countries as long as the GM crop under review: 1) had been studied under different environmental conditions; 2) behaves in the same way as its conventional counterpart; 3) was not a crop for which Paraguay was center or origin; 4) does not have relationship to known weeds in Paraguay that could cross-breed; and 5) was assessed in the context of plant pests known in Paraguay.[31] Soon after this regulation, thirteen GM crop events were approved in Paraguay.[31] A timeline for the above history of GM crop approvals and Regulations in Paraguay through 2019 is shown in Figure P1.

In 2019, Paraguay published a resolution outlining regulatory processes for GED crops and other new plant breeding techniques (NPBTs). MAG published Resolution No. 565, "Form of Prior Consultation for products obtained through new techniques of genetic improvement" on May 13, 2019.[13]

Under this resolution, CONBIO was set as the responsible body for review of NPBTs, including GED crops. For GED crops and determination of their non-GMO regulatory status, applicants must provide information on the biology of the modified organism, the breeding methodology used, the targeted DNA sequences and their functions in the organism prior to and after genome editing, the sequence of the DNA constructs employed in NPBTs, an analysis of off-target effects, evidence of no rDNA in the final product, analyses of any potential unintended effects on phenotypes or changes in proposed uses of the organism, and any recommended changes in managing the organism.[13]

ix Note: some authors and reports use different acronyms for this Commission, including COMBIO and CNTBio. We use the acronym listed in MAG (2012).

Like Brazil's resolution, Paraguay names certain NPBTs in its resolution.[15] It seems that decisions will be made on a case-by-case basis, also taking into consideration whether the GED crop has been approved in another country.

Paraguay is likely not to regulate GED crops as GMOs as long as there is no foreign DNA present in the final product.[13,37] Also, Paraguay declared its intention to take a similar approach to Argentina, Uruguay, and Brazil towards NPBTs and GED crops in a resolution to the WTO.[13]

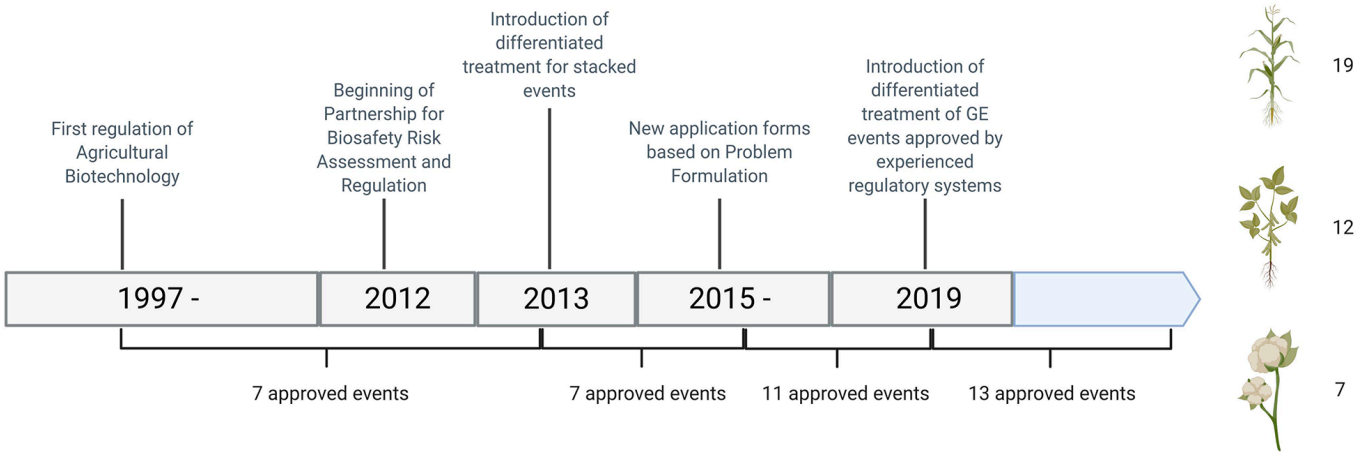


FIGURE 1 | Number of GE events approvals in Paraguay from 2004 to 2019, divided by stage of development of the regulatory system.

Figure P1. Paraguay's History of Biotech Crop Regulation and Approvals. From (Candia et al. 2020).

H. PERU

Peru established Law No. 27104, "Law of Prevention of Risks Derived from the Use of Biotechnology" in May 1999. One year prior to Peru joining the Cartagena Protocol. The law is designed to: 1) protect human health, the environment, and biological diversity; 2) promote biosafety in both research and development of biotechnology; 3) regulate, administrate, and control the risks derived from the use of confined and released LMOs; and 4) regulate the interchange and commercialization of LMOs, inside the country and as well as throughout the world. The law covers research, production, introduction, manipulation, transport, storage, conservation, interchange, commercialization, confined use, and liberation of LMOs, as well as any activity that involves the manipulation of molecules of recombinant deoxyribonucleic acid (DNA) or the use of LMOs as vectors, either as recipients or donors.[38] The National Biosafety Framework, released in 2005, provides a framework for "managing activities to guarantee biosafety in relation to LMOs or their derived products" via a case by case risk assessment and brings Peru into compliance with the CPB which it ratified in 2004.[38]

In 2011 Law 29811 was approved which established a 10-year moratorium on the "cultivation of genetically engineered organisms." This was followed by Supreme Decree 008-2012-MINAM, which established the implementing regulations for Law 29811.39 This law was extended for another five years in 2020. The law provides three exemptions: 1) laboratory research; 2) use in pharmaceuticals and veterinary products; and 3) use in food, animal feed, and in food processing. One of the laws aims to develop a nationwide inventory of animals, plants, insects, and soil microorganisms that could be impacted by GMOs. Dialogues pertaining to biotechnology are conducted within the National Committee of Biological Diversity, which should also include genome editing. This committee encompasses regulatory agencies, academia, industry, and international organizations like the International Potato Center.[40] Supreme Decree 008-2012-MINAM establishes definitions for both living modified or-

ganisms and transgenes, which could impact future discussions around genome editing; particularly the inclusion of *"synthetic gene"* in the definition of a transgene.

› **Living Modified Organisms**: Any living organism that possesses a new combination of genetic material that has been obtained through the application of modern biotechnology.[39]

› **Transgene**: Gene sequence inserted into an organism to transform it and that is inheritable. The transgene may come from a different species than the receptor or a *synthetic gene*.[39]

According to the USDA Foreign Service, there is interest amongst the scientific community within Peru around genome editing.[40] As of this writing, Peru has not made a distinction for genome editing as it relates to Supreme Decree 008-2012-MINAM and the moratorium on GMOs.

I. URUGUAY

Uruguay is highly dependent on agricultural trade and is the 6th largest exporter of soybeans, behind Brazil, the U.S., Argentina, Paraguay, and Canada.[30] Agriculture represents 10% of Uruguay's GDP and 67% of the country's total exports are agricultural products.[41] The main agricultural sectors are beef, soybeans, and forestry. Uruguay now ranks 11th among countries in the number of hectares planted with biotech varieties.[9] Authorized biotech events for production and commercialization in Uruguay include several GM corn and soybean varieties. Bt and Ht GM crops have had a high penetration in Uruguay with over 99% soy and 90% corn planted in GM varieties.[41]

The first GM crop applications for approval occurred in Uruguay in 1995, when the General Direction of Agricultural Services (DGSA) of the Ministry of Livestock, Agriculture and Fisheries (MGAP) issued a resolution establishing a procedure for risk analysis after GM corn and Round-up Ready (RR) soybean applications were submitted. An Advisory Committee for Risk Analysis (CAAR) was convened under MGAP to review the applications and advise MGAP on these approvals. In 2000, the regulatory system was further formalized by Decree 249/000 to create the Commission on Risk Assessment of Genetically Engineered Plants (CERV) which was composed of representatives from the Ministries of Agriculture, Environment, and Health, as well as the National Institute of Seeds (INASE) and the National Agricultural Research Institute (INIA).[42] Decree 249/00 established a regulatory framework to authorize the introduction, use, and manipulation of GMOs.[41]

In 2007, the Government of Uruguay put forth a moratorium to suspend approvals until a new regulatory framework could be put into place. CERV stopped functioning formally and a governmental inter-ministry working group (GIM) was convened to review and adjust the regulatory system established under Decree No. 249/000. GIM developed a proposal for a biosafety framework, which was adopted in 2008 under the Decree No. 353/008, thus revoking the prior Decree 249/000. In 2009, Uruguay again began to approve field tests of new GM corn and soybean varieties specifically for field testing, commercialization, and exportation. In 2012, the government also changed its policy on granting the renewal of permits for GM varieties used for exportation purposes only. The process was speeded up, as the authority to grant renewals was given to the Political Commission, who prior to this advised the Ministries, who then would grant the renewals. These efforts paved the way for greater biotech crop adoption in Uruguay.

Authorizations for GMOs under the National Biosafety Cabinet (GNBio) are granted for laboratory use, field trials, commercialization, and export. Approvals from other countries that follow the same technical criteria are considered as a precedent in the approval evaluation process, e.g., Argentina, Brazil, the United States, Canada, Australia, the European Union among others.[41]

To date, Uruguay has no specific regulations for NPBTs or gene-edited crops.[13,37] However, in 2018, Uruguay joined other countries, including Argentina, Australia, Brazil, and the U.S. among others (Table 2), in a joint statement to the World Trade Organization which promoted relaxed regulations for genome editing, stating that governments should "avoid arbitrary and unjustifiable distinctions" between GED crops and conventionally bred crops.[13,43] Other reports classify Uruguay's approach to GED crops (or NPBTs) as probably similar to Paraguay's "likely case-by-case: if no foreign DNA then not regulated as GMO." While not official as of this writing, Uruguay also has expressed an interest in adopting a similar approach to Argentina and Brazil.[37]

There are emerging capacities in Uruguay for research and development of GED crops. Public institutions in Uruguay, such as the Universidad de la República and Instituto Nacional de Investigación Agropecuaria (INIA) are developing CRISPR-edited crops such as herbicide-resistant soybean, reduced-lectin in soybean, and mandarin and tomato with more lycopene.[13]

III. DISCUSSION

The LAC region appears to be coalescing around a particular viewpoint on genome editing as it relates to LMOs (see Table 2 and Figure 1), specifically that many GED products will not be regulated as GMOs. Argentina was the first in the region with Brazil, Chile, Colombia, Paraguay, Honduras, and Guatemala following suit.[13] (Table 2 and Figure 3)

As most countries in the region are signatories to the Convention on Biological Diversity, Cartagena Protocol, and some have signed onto the World Trade Organization's statement on genome editing (see Table 2/Box 1), how this will impact negotiations on the global level, specifically within the Convention on Biological Diversity and its' Cartagena Protocol when other regions in the world (European Union) and other countries within the LAC region have taken different positions remains an open question. Examining these specific differences and how they may impact future international discussions will be important to track over time.

Country	Party to Cartagena Protocol on Biosafety	GMO regulation	Genome editing specific regulations	Signature to WTO precision biotech statement (See Box 1.)
Argentina	No	Yes	Yes—2015	Yes
Bolivia	Yes	Yes	No	No
Brazil	Yes	Yes	Yes—2018	Yes
Colombia	Yes	Yes	Yes—2018	No
Honduras	Yes	Yes	Yes—2019	Yes
Mexico	Yes	Yes	No	No
Paraguay	Yes	Yes	Yes—2019	Yes
Peru	Yes	Yes (current ban on all GMOs)	No	No
Uruguay	Yes	Yes	No	Yes

Table 2. Overview of Gene edited crop oversight in select LAC countries.

BOX 1. WTO (WORLD TRADE ORGANIZATION)— INTERNATIONAL STATEMENT ON AGRICULTURAL APPLICATIONS OF PRECISION BIOTECHNOLOGY

Communication from Argentina, Australia, Brazil, Canada, The Dominican Republic, Guatemala, Honduras, Paraguay, Philippines, The United States of America and Uruguay.

From (WTO - Committee on Sanitary and Phytosanitary Measures 2020)

Agricultural innovation has played an essential role in increasing yields and productivity in support of growing, prosperous civilizations. Innovations in precision biotechnology, such as gene editing, have brought the promise of major improvements in terms of the ease and precision of introducing desirable traits into agricultural organisms, as compared to other breeding methods. Farmers continually need to broaden access to new tools to improve productivity, plant and animal health, and environmental sustainability, and need to help address global challenges such as climate change, pest and disease pressures, and the safety and security of worldwide food supplies, as well as meet consumer preferences and demands for healthier, higher quality foods at affordable prices. Government policies must continue to foster innovation, including in the public sector and by small and medium-sized enterprises (SMEs), and mitigate unintended, unnecessary barriers to the entry of agricultural products.

In some cases, precision biotechnology, such as gene editing, may generate organisms with characteristics similar to those obtainable through conventional breeding. In other cases, the organisms generated may have characteristics similar to those introduced into organisms using recombinant-DNA technologies. In either case, the food, animal, and environmental safety of such products can be adequately addressed by existing regulatory frameworks for agricultural products and existing safety standards based on the characteristics of the product or organism.

Governments are engaging in policy discussions on regulatory frameworks and global regulatory compatibility to encourage cross-border research collaboration and minimize potential disruptions to trade. Differing domestic regulatory approaches for products derived from precision biotechnology may result not only in international a synchronicity in approvals, but also in asymmetry in regulatory approaches, and create potential trade issues that could impede innovation.

BOX 1. CONT.

Recognizing the potential positive contributions of precision biotechnology to global agriculture, and emphasizing the importance of early action to identify avenues to minimize the trade impacts of differing regulatory approaches, the undersigned governments acknowledge that:

› Precision biotechnology products have the potential to play a critical role in addressing the challenges facing agricultural production, including by contributing to increasing the supply of foods and other agricultural products, in a sustainable way;

› Collaborative research efforts and the ability to introduce useful products into the market, especially by SMEs and public sector researchers, are necessary to fully realize the potential of precision biotechnology;

› Given the differences internationally in approaches used to assess agricultural biotechnology, due consideration should be exercised by governments to avoid arbitrary and unjustifiable distinctions between end products derived from precision biotechnology and similar end products obtained through other production methods;

› To ensure appropriate science- and risk-based approaches consistent with the protection of human, animal and plant health and the environment, due consideration should be given to available scientific and technical information when updating existing regulatory frameworks or applying these frameworks to products of precision biotechnology, and when using available flexibility within existing regulatory frameworks for agricultural products;

› Regulatory approaches necessary to help ensure safety (of humans, animals, plants, and the environment) in respect of products derived from precision biotechnology should be science- and risk-based, transparent, predictable, timely, and consistent with relevant international trade obligations;

› Cooperative work by governments to minimize unnecessary barriers to trade related to the regulatory oversight of products of precision biotechnology, including the exploring of opportunities for regulatory and policy alignment, should be pursued where possible;

› This collaborative work should promote constructive dialogue with trading partners and agricultural stakeholders on potential trade issues related to precision biotechnology, so as to support open and fair trade and encourage research and innovation;

› Public communication efforts can build trust in regulatory frameworks and improve the acceptability of future agricultural innovations that will help farmers address global challenges with a view to the production of abundant, safe and affordable food, feed, fibers, and energy in the 21st century.

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Acknowledgements

INTER-AMERICAN DEVELOPMENT BANK

Funding for this project, "Assessment of the Regulatory and Institutional Framework for Gene-editing via CRISPR-based Technologies in Latin America and the Caribbean" provided by the Inter-American Development Bank, project number RG-T3431. IDB works to improve lives in Latin America and the Caribbean. Through financial and technical support for countries working to reduce poverty and inequality, IDB helps improve health and education, and advance infrastructure to achieve development in a sustainable, climate-friendly way.

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The consultancy team includes experts from economics, public policy, international law, communications, and biotechnology.

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