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REVIEW

Biosafety legislation and the regulatory status of the products of precision breeding in the Latin America and the Caribbean region

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Societal Impact Statement

Precision breeding represents a new challenge for biosafety regulators when applying the legal definition of living modified organisms (LMOs) in accordance with their domestic biosafety legislation. Globally, there is uncertainty whether the products of precision breeding will be considered as LMOs and subject to the corresponding regulatory oversight. This article illustrates current regulatory matters of precision breeding in all Latin American and Caribbean countries, serving as a baseline contributing to further discussions about the potential future regulatory status of precision breeding products and its corresponding socioeconomic and environmental impact in the region.

Summary

It is still uncertain whether the products of precision breeding will be considered and regulated as living modified organisms (LMOs) or not. This article illustrates current regulatory matters of precision breeding in the Latin America and the Caribbean (LAC) region and provides recommendations to support the corresponding legal interpretation. This is done by analyzing domestic biosafety legal frameworks of LMOs, together with the results from a survey sent to regulatory officers and public researchers in the region. Previous similar publications have focused on a limited selection of countries in the region, but this is the first time a comprehensive overview of all 33 countries is presented. Our results classify countries in five main groups based on their approach to define LMOs under domestic biosafety legislation. Most notably, the key criterion for the clustering of countries is whether the legislation has adopted the legal definition of LMOs according to the Cartagena Protocol on Biosafety to the Convention on Biological Diversity or not. This article highlights that the lack of clarification on the meaning of major terms, such as "naturally," "manipulation," and "a novel combination" of genetic material, can provoke ambiguity when applying the biosafety law in products derived from precision breeding. Also, countries require to adopt administrative procedures to determine the regulatory status of precision breeding products. Finally, this article suggests that the rapid adoption of such procedures relevant to

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precision breeding is strongly connected to the role of agriculture and biotechnology in the countries and with national economic and political perspectives.

El mejoramiento genético de precisión representa un nuevo desafío para los reguladores en bioseguridad cuando aplican la definición legal de Organismo Vivo Modificado (OVM) de acuerdo con sus leyes nacionales en bioseguridad. A nivel mundial, existe incertidumbre sobre si los productos derivados del mejoramiento genético de precisión serán considerados OVMs y si serán sujetos a la correspondiente supervisión regulatoria. Este artículo ilustra los asuntos regulatorios actuales del mejoramiento genético de precisión en todos los países de América Latina y el Caribe. Así, este artículo sirve como línea base para contribuir a las posteriores discusiones sobre el estado regulatorio potencial y futuro de los productos derivados del mejoramiento genético de precisión y sobre sus impactos socio-económicos y ambientales correspondientes en la región.

KEYWORDS

biosafety law, biotechnology, Cartagena Protocol on Biosafety, Latin America and the Caribbean, living modified organism, precision breeding

1 | INTRODUCTION

The Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity (CBD) is an international agreement that aims to protect biological diversity by ensuring the safe handling, transport, and use of living modified organisms (LMOs) resulting from modern biotechnology (Secretariat to the Convention on Biological Diversity, 2000). Most of the concepts and provisions of the CPB are present in similar forms in the domestic biosafety instruments of most countries (Frison et al., 2013). For instance, most countries have included the CPB's LMO definition in their biosafety legal frameworks to regulate the use of LMOs in their territories (Whelan & Lema, 2015). In certain jurisdictions, however, a somewhat different definition has been adopted that may or may not align in every respect with the LMO definition of the CPB. For example,

- "Plants with novel traits" are regulated in Canada according to the Directive 94-08 (Canadian Food Inspection Agency, 2018),
- the United States of America (USA) regulates "genetically engineering organisms" as stipulated in the Coordinated Framework for Regulation of Biotechnology (Office of Science and Technology Policy, 1986), and
- the European Union (EU) regulates "genetically modified organisms" (GMOs) based on Directive 2001/18/EC (Official Journal of the European Communities, 2001).

Precision breeding, alternatively called "new breeding technologies" or "new genomic techniques," represents a new challenge for biosafety regulators when applying the legal definition of LMO in accordance with their domestic biosafety legislation. This is a consequence of some of these techniques resulting in organisms and products that cannot be distinguished from their conventionally developed counterparts. For instance, according to the United State Department of Agriculture (USDA), genome editing techniques may produce new plant varieties that are indistinguishable from those developed through traditional breeding methods (USDA, 2018). Many plants produced by genome editing are therefore not subject to regulation by USDA once the editing construct has been crossed out (Schmidt et al., 2020).

In other countries, currently, there are claims that products of precision breeding under certain conditions should be excluded or exempted from the biosafety legislation (Lusser et al., 2011). For example, in the EU, some authors claim that if the breeding process has not resulted in any genetic alteration that does not occur naturally, the final product cannot be considered as GMO in accordance with the legal definition of a GMO in the EU (Sprink et al., 2016; van der Meer et al., 2021). However, with the recent ruling of the Court of Justice of the EU, new mutagenesis techniques result in products that are subject to the provisions of the GMO regulatory framework, and this has led to the interpretation by many that also all genome-edited organisms must be regulated as GMOs (Schmidt et al., 2020).

Overall, it is in this context often unclear whether either the technique itself or the resulting genetic alteration, or both, is the trigger for regulation by current LMO biosafety legislation in a given jurisdiction (Hartung & Schiemann, 2014; Sprink et al., 2016). As a result, most countries, specially CPB Parties, require legal clarity to the regulatory status of precision breeding (Gatica-Arias, 2020). In other words, whether products derived from precision breeding will be included under the LMO definition or not (Gatica-Arias, 2020). Around the world, only a few countries have enacted and/or modified legal instruments towards the regulation of products derived from precision breeding in plants (Schmidt et al., 2020).

1.1 | Biosafety in the Latin America and the Caribbean

In the Latin America and the Caribbean (LAC) region, most countries are CPB Parties (United Nations Treaty Collection, 2020) and, as such, have adopted the legal definition of LMO in accordance with the CPB. However, the LAC countries are very heterogeneous in terms of adopting biosafety legal frameworks and R&D activities on LMOs (Araya-Quesada et al., 2012). Clearly, political and economic contexts are important factors influencing technological development and the range of economic profit, and societal need determines technological priorities (Mitchell & Bartsch, 2020).

For example, some countries such as Argentina, Brazil, Chile, Colombia, Cuba, Honduras, Mexico, Paraguay, and Uruguay have operational biosafety regulatory systems since the 1990s and have authorized the use of LMOs for different purposes (Rosado & Craig, 2017). In fact, most of these countries are major exports of LMOs including key agricultural commodities such as soybean, cotton, and maize (ISAAA, 2019). In addition, most of these countries have recently adopted legal provisions to recent technical developments in precision breeding (Gatica-Arias, 2020). Clearly, this is a response of a growing interest by such countries in these advances in plant biotechnology (Eriksson et al., 2019).

To the contrary, other LAC countries, such as Bolivia, Ecuador, Peru, and Venezuela, have adopted domestic legislative measures to ban the cultivation and commercialization of LMOs (Rosado & Craig, 2017). For instance, Peru has recently approved the extension of its moratorium law on the entry and cultivation of LMOs till 2035 (Official Journal El Peruano, 2021). Also, most Caribbean countries are in the early stages to develop biosafety bills (Rosado & Craig, 2017).

1.2 | Purpose of this study

The purpose of this study is to survey the current regulatory status of precision breeding and its derived products or organisms in all 33 countries of the LAC region and provide legal and technical recommendations, if needed, to support the corresponding legal interpretation. This will be done by analyzing domestic biosafety legislation and regulations of LAC countries together with the results from a survey to regulatory officers and public researchers in the region. The biosafety legislation applies commonly to all types of organisms, with the exception of human beings; however, this study will largely focus on plants as this is the organism group for which there is most research and regulatory experience in the LAC region. It is the first time such a comprehensive study is performed to cover the entire LAC region.

2 | MATERIALS AND METHODS

This study was primarily conducted through a consultation of regulatory officers and publicly funded researchers, composed by online surveys (Tables S1 and S2) using the freely available Google Forms tool. Key people closely involved in the implementation of the CPB and domestic biosafety legislation, and R&D activities on LMOs and precision breeding in the LAC region were targeted. The composition of the LAC geographical region is designated in accordance with the United Nations (United Nations Statistics Division, 2020).

First, a contact database of approximately 100 people was developed including two categories of stakeholders: (i) representatives of National Competent Authorities (NCAs) and governmental agencies, including CPB and Biosafety Clearing-House National Focal Points, from all 33 LAC countries and (ii) researchers from universities and international and national research centers of 17 countries (no contact information was found for researchers working on precision breeding in the remaining 16 countries). Second, online surveys in both Spanish and English were designed specifically for each target category. Each survey form included yes/no, multiple choice and open-ended questions on technical, regulatory and legal aspects of precision breeding (see survey questions in Table S1 [for regulators] and Table S2 [for researchers]). Online surveys were circulated to each contact between November 2019 and February 2020.

The data returned from respondents of the first category of stakeholders belonged to 19 representatives of NCAs and governmental agencies covering 18 countries (Table S3). For the second category of stakeholders, data were returned from 20 individual researchers from research institutions in 13 countries (Table S4). Information on the countries that we could not cover through the survey was collected by a revision of domestic legislation and regulations of precision breeding and biosafety of LMOs from national gazettes and by recent peer-reviewed literature.

The names of the institutes were translated from Spanish or Portuguese to English by the authors; however, their acronyms were written in their official language. Translations of legal material from Spanish to English were made by the authors, with Spanish being the native language of AR.

For the purpose of this study, we have used the term "precision breeding" as synonymous to the terms "new breeding techniques," "new plant breeding techniques," or "new genomic techniques." Though there is not yet any widely recognized definitions on any of these terms, they have often been used to cluster a number of techniques developed in the past two decades and for which the legal status of the derived products in relation to any given LMO regulatory framework may be unclear (see explanation in Table 1).

2.1 | Rationale for the clustering of countries

Most LAC countries are CPB Parties, with the exception of Argentina, Chile and Haiti (United Nations Treaty Collection, 2020). LMO and modern biotechnology are legal terms defined by the CPB, and therefore, they are accepted terms by most jurisdictions and have been incorporated into domestic law. Regardless of their adherence to the CPB though, most LAC countries have adopted the LMO and modern biotechnology definitions based on Art. 3 of the CPB and few others have adopted a different definition to regulate GMOs.

TABLE 1 Definitions of key terms relevant to determine the regulatory status of precision breeding products

Terms	General definition and interpretation
Living modified organism (LMO)	Art. 3(g) of the CPB defines "LMO" as "any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology" (Secretariat to the Convention on Biological Diversity, 2000). Clearly, this definition refers both to the technique ("modern biotechnology") and the end product ("an organism that possess a novel combination of genetic material") in a cumulative way (Fernandez & Van der Meulen, 2018). For some authors, the CPB's LMO definition is interpreted by two considerations: a process-based trigger, by means of the use of the indicated techniques of modern biotechnology, and a product-based trigger, as the resulting organism, or its derived product, possesses a novel combination of genetic material obtained in a different way than conventional, traditional or natural (Custers et al., 2019).
Modern biotechnology	Art. 2 of the CBD defines "biotechnology" as any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify (United Nations, 1992). Specifically, Art. 3(i) of the CPB defines "modern biotechnology" as the application of (i) in vitro nucleic acid techniques, including recombinant DNA and direct injection of nucleic acid into cells or organelles or (ii) fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection (Secretariat to the Convention on Biological Diversity, 2000). For instance, recombinant DNA and associated techniques include the array of techniques used to isolate, cultivate, purify, replicate, and convert DNA sequences and other biological products such as lower and higher life forms, cells lines, and plasmids (Pila, 2003).
Precision breeding	There is no international consensus on the definition of precision breeding nor a list of technologies that are exclusively categorized as precision breeding (Whelan & Lema, 2015). However, the following techniques were listed by the New Techniques Working Group of the European Commission in 2007 (NTWG, 2012) and are also, though some of them are radically different from one another and with little in common, and some currently not even used directly for plant breeding, extensively described by many authors (Friedrichs et al., 2019; Lusser et al., 2011; Sprink et al., 2016), comprising (i) genome editing techniques, such as oligonucleotide-directed mutagenesis (ODM) or site-directed nucleases (SDNs), (ii) epigenetic modification, such as RNA-directed DNA methylation (RdDM), (iii) agroinfiltration, (iv) cis-/intra-genesis, (v) grafting with GM material, (vi) reverse breeding, (vii) RNA interference (RNAi), and (viii) synthetic biology. Also, gene drive systems can now be added to the list (Rode et al., 2019). Some of them are procedural technologies whereas others can be more considered as conceptual (Hartung & Schiemann, 2014). It can be argued that regular GMOs/LMOs also constitute a type of precision breeding, given the high degree of control in trait management through recombinant DNA technologies. However, for the purpose of legal considerations, the concept of precision breeding has often been used to denote those technologies that have developed more recently and for which the regulatory status of the resulting products may be unclear.

Therefore, this study divides the LAC countries in two main clusters, with a total of five subgroups, based on their approaches to define LMOs under domestic legislation according to international environmental law provisions, most notably the CPB. The first consideration to classify LAC countries is whether they incorporate the CPB's LMO definition into domestic biosafety legislation or not. For the countries that have adopted the CPB's LMO definition, a subgrouping is made based on the robustness of their biosafety legal frameworks, most notable whether legal provisions relevant for the products of precision breeding have been implemented or not. For the countries that do not follow the CPB's LMO definition and instead regulate GMOs, a subgrouping is made to explore the kind of approach to define GMO based on their biosafety domestic legislation.

To initially explore whether products derived from precision breeding will fall under biosafety oversight at a national level in the LAC region, attention must be given to three key terms, namely, LMO, modern biotechnology, and precision breeding under current biosafety domestic legislation. Based on such definitions, preliminary assumptions can be developed to analyze whether precision breeding products will fall under biosafety regulations in the targeting jurisdictions regardless the adoption of regulations to determine the regulatory status of precision breeding products.

Table 1 provides an explanation of legal definition including LMO and modern biotechnology based on international environmental law, precisely by Art. 3 of the CPB. Also, as there is no global legal definition for precision breeding, Table 1 explain what the term precision breeding means based on scientific information. It is important to note that there is no binding definition of LMO, modern biotechnology, or precision breeding developed by any intergovernmental organization in the Americas, including, inter alia, the Organization of American States (OAS), The Caribbean Community (CARICOM), The Andean Community (CAN), The Southern Common Market (MERCOSUR), and The Central American Integration System (SICA).

3 | RESULTS

3.1 | First cluster: Countries that adopt, or are in the process of adopting, the CPB's LMO definition

In the LAC region, 16 countries (Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, Guatemala, Honduras, El Salvador, Mexico, Nicaragua, Paraguay, Peru, Uruguay, and Venezuela) have incorporated the CPB's LMO definition into domestic

TABLE 2 Survey results: State-of-the-art of precision breeding in LAC countries of the first cluster (e.g., countries that adopt or will adopt the CPB's LMO definition)

		Precision breeding		
Classification of countries	**Country**	**Legal provisions**	**R&D activities**	**Biosafety legal framework for LMOs**
Subgroup I: Countries with legal provisions addressing precision breeding	Argentina	Yes, since 2015. MAGYP Resolution 173/2015 (Official Journal of Argentina, 2015).	The National Institute on Agricultural Technology (INTA) is doing research under containment on different crops, comprising cereals, pulses, oil crops, root and tuber crops, forage crops, fruit and berry crops and fiber crops, using the following techniques: genome editing techniques, epigenetic modification, gene drive systems, agroinfiltration, grafting, RNAi, and synthetic biology. Additionally, the University of Buenos Aires (UBA) are currently doing confined trials on bovines with genome editing techniques.	Yes. Resolution 701/2011 (Official Journal of Argentina, 2011).
	Brazil	Yes, since 2018. CTNBio Normative Resolution 16 (Official Journal of the Federal Government of Brazil, 2018).	Federal University of Pernambuco (UFPE) investigates cereals and forage crops, including sugar cane, using genome editing techniques and synthetic biology under containment.	Yes. Biosafety Law 11.105 (Official Journal of the Federal Government of Brazil, 2005).
	Chile	Yes, since 2017. SAG Consultation Form (SAG, 2017)	Technologies, including genome editing techniques, epigenetic modification, gene drive systems, agroinfiltration, grafting, RNAi, synthetic biology, and cis-/intra-genesis, are being used in cereals, root and tuber crops, fruit and berry crops in contained facilities by the Agriculture and Livestock Research Institute (INIA).	Yes, since 2001. Resolution 1523/2001 (Official Journal of Chile, 2001).
	Colombia	Yes, since 2018. ICA Resolution 00029299 (Official Journal of Colombia, 2018).	Oil crops are investigated by techniques, under containment, such as agro-infiltration, cis-/intra-genesis and synthetic biology at the EAFIT University. Also, International Center for Tropical Agriculture (CIAT) investigates in cereals, pulses and root and tuber crops using genome editing techniques in contained and confined facilities.	Yes, since 2002. Biosafety Law 740 (Official Journal of Colombia, 2002).
	Paraguay	Yes, since 2019. MAG Resolution 565 (Official Gazette of Paraguay, 2019).	Genome editing techniques are being used in oil crops under containment at the National University of Asuncion	Yes, since 2012. Decree 9699 (Official Gazette of Paraguay, 2012).

TABLE 2 (Continued)

Classification of countries	Country	Precision breeding		Biosafety legal framework for LMOs
		Legal provisions	R&D activities	
			(UNA). In addition, Institute of Agricultural Technology (IPTA) has stated to investigate root and tuber crops using genome editing techniques under containment.	
	Guatemala	Yes, since 2019. Ministerial Resolution of the Customs Union 60/2019 (Central American Journal of Guatemala, 2019).	No information found (NIF)	Yes. Ministerial Agreement 386-2006 (Central American Journal of Guatemala, 2006).
	Honduras	Yes, since 2019. Ministerial Resolution of the Customs Union 60/2019 (Central American Journal of Guatemala, 2019).	The National Autonomous University (UNAH) is currently doing confined field trials on cereals using synthetic biology.	Yes, since 2001. Biosafety Regulation 1570-98 (The Gazette Official Journal of Honduras, 2001).
Subgroup II: Countries taking initial steps toward a legal approach to precision breeding	Costa Rica	Under initial discussions in the National Committee on Biosafety	Genome editing techniques are being used in cereals under containment at the University of Costa Rica (UCR).	Yes, since 2006. Law 8537 (The Gazette Official Journal of Costa Rica, 2006).
	Dominican Republic	Under initial discussions in the National Technical Commission on Biosafety	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	Yes, since 2015. Law 219-15 (Official Gazette of Dominican Republic, 2015).
	Ecuador	Regulations are under development by the Ministry of Environment (MAE)	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	Yes, since 2015. Ministerial Agreement 013 (Official Registry of Ecuador, 2015).
	El Salvador	Regulations are under development by the Ministry of Environment and natural resources (MARN)	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	Yes, since 2008. Decree 78 (Official Journal of El Salvador in Central America, 2008).
	Mexico	Under initial discussions	There are governmental institutions authorized to use precision breeding techniques in cereals and oil seeds under containment.	Yes, since 2005. Law DOF 18-03-2015 (Official Journal of the United Mexican States, 2005).
	Nicaragua	NIF	NIF	Yes, since 2010. Law 705 (The Gazette Official Journal of Nicaragua, 2010).
	Peru	Regulations are under development by the Ministry of Environment (MINAM)	National Institute of Innovation in Agriculture (INIA) is doing studies under containment with the use of genome editing techniques on root and tuber crops, fruits and berry crops.	Yes, since 1999. Law 27104 (Official Journal El Peruano, 1999).
	Uruguay	NIF	The University of La Republica (UDELAR) carries out research activities in	Yes, since 2008. Decree 353/008 (Official Journal of Uruguay, 2008).

(Continues)

TABLE 2 (Continued)

Classification of countries	Country	Precision breeding		Biosafety legal framework for LMOs
		Legal provisions	R&D activities	
			contained facilities on cereals and pulses by the use of genome editing, agroinfiltration, cis-/intra-genesis and RNAi.	
	Venezuela	Under initial discussions	Foundation Institute of Advances Studies (IDEA) is initially studying the use of genome editing techniques on cereals in laboratories.	Yes, since 2015. Seeds Law 6.207 (Official Gazette of Venezuela, 2015).
Subgroup III: Countries currently drafting biosafety frameworks	Antigua and Barbuda	Regulations are under development by the Ministry of Agriculture, Fisheries and Barbuda Affairs	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	No. Currently under development.
	Grenada	Regulations are under development by the Ministry of Agriculture, Lands, Forestry and Fisheries	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	No. Currently under development.
	Saint Lucia	Under initial discussions	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	No. Currently under development.
	Suriname	Under initial discussions	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	No. Currently under development.
	Barbados	None	NIF	No. Currently under development.
	Belize	None	NIF	No. Currently under development.
	Dominica	None	NIF	No. Currently under development.
	Guyana	None	NIF	No. Currently under development.
	Haiti	None	NIF	No. Currently under development.
	Saint Vincent and the Grenadines	None	NIF	No. Currently under development.
	The Bahamas	None	NIF	No. Currently under development.
	Trinidad and Tobago	None	NIF	No. Currently under development.

Note: Contained use refers to activities in laboratories, glasshouse, and greenhouse, and confined use makes reference to activities in confined field trials.

biosafety legislation (Table 2; Figure 1). In addition to those countries, 12 Caribbean countries (Antigua and Barbuda, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Saint Lucia, Saint Vincent and the Grenadines, Suriname, The Bahamas, and Trinidad and Tobago) are currently developing biosafety bills that will include the LMO and modern biotechnology definitions as stated in Art. 3 of the CPB (Table 2). Among all these 28 LAC countries, only a few of them have adopted legal provisions, such as regulations and enquiry forms, relevant for precision breeding. These instruments have the main purpose to determine the regulatory status of precision breeding products and ensure whether such products will fall under LMO biosafety regulation or not.

3.1.1 | Subgroup I: Countries with legal provisions addressing precision breeding

Seven Latin American countries (Argentina, Brazil, Chile, Colombia, Guatemala, Honduras, and Paraguay) have a biosafety legal framework of LMOs, which include specific provisions addressing the regulatory status of precision breeding and the derived products (Gatica-Arias, 2020). Argentina, Brazil, Chile, and Colombia, as well as most recently Paraguay, have established fairly similar regulations (Lema, 2019). Guatemala and Honduras have adopted a bilateral agreement only to regulate the commercial exchange of LMOs for agricultural and livestock purposes between both countries, including certain provisions related to the regulatory status of precision breeding. It is important to point out that such bilateral agreement between Guatemala and Honduras, including its definitions, so far only has jurisdiction on the bilateral trade occurring between both countries. Third countries that wish to introduce products of certain breeding techniques in these countries have to follow the domestic biosafety legislation of each country.

Survey results on regulatory matters

Argentina, Brazil, Chile, Colombia, Guatemala, Honduras, and Paraguay have adopted regulations to establish administrative procedures and to approve application forms to receive queries from applicants to assess the regulatory status of precision breeding products. In general terms, these regulations establish an early consultation procedure to determine when a crop, obtained using precision breeding techniques including techniques of modern biotechnology, is subject to regulation by domestic LMO legislation. Overall, the application forms or consultation forms request information of the final product and the technology used, including information related to

- data about the parental organism, such as its molecular biology and phenotype,
- the breeding methodology used to obtain and select the crop including the new trait or introduced characteristic, and an indication of the modified DNA sequences,

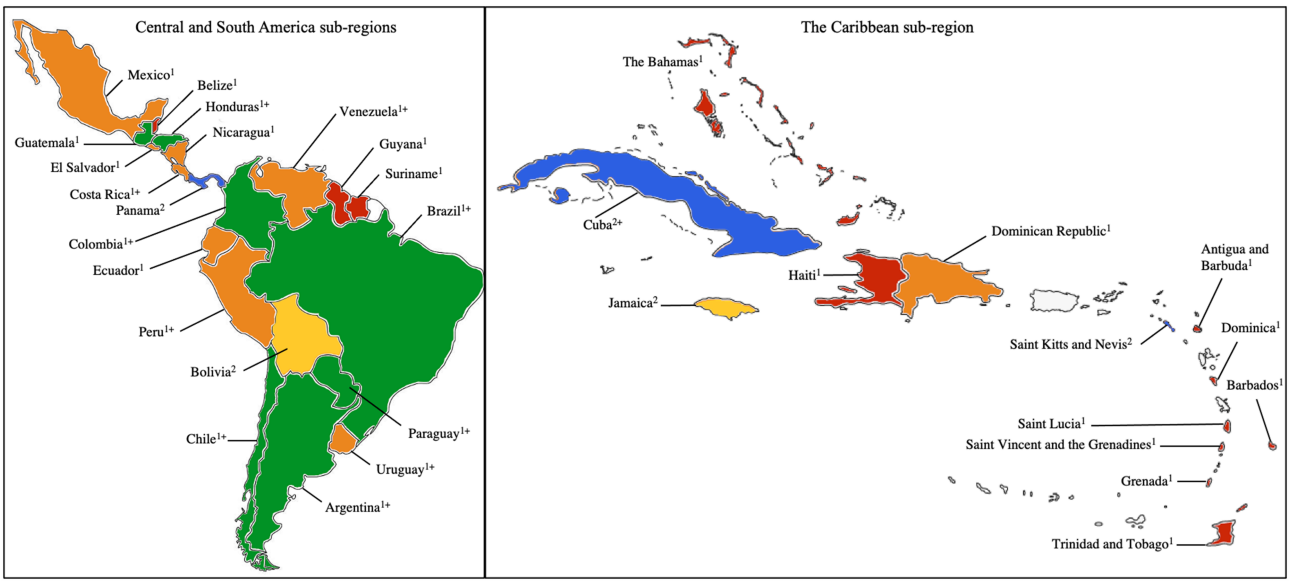

FIGURE 1 Classification of LAC countries based on results of the stakeholder consultation on precision breeding. *Note*. Numbers, ([1]) = first main cluster, countries that/will adopt the CPB's LMO definition; ([2]) = second main cluster, countries that do not define LMOs as the CPB. Colors, in green = subgroup I, countries with legal provisions relevant to precision breeding; in orange = subgroup II, countries taking steps toward a legal approach to precision breeding; in red = subgroup III, countries currently drafting biosafety legislation; in blue = subgroup IV, countries that define GMOs similar to the EU; in yellow = subgroup V, countries with a different GMO definition, and in white: overseas territories not part of this study. Symbols, ([+]) = countries in which research institutions are dealing with R&D activities using precision breeding technologies

- evidence of stably inherited genetic changes in the final product, including technologies used to discard a stably inserted new combination of genetic material in the final product/organism, and
- information about prior authorizations of the requested crop in other countries (applicable for Chile and Colombia only).

NCAs in these seven countries (e.g., Ministry of Agriculture, Livestock and Fisheries [MAGYP] in Argentina, National Biosafety Technical Commission [CTNBio] in Brazil, Service for Agriculture and Livestock [SAG] in Chile, Colombian Institute of Agriculture and Livestock [ICA] in Colombia, Ministry of Agriculture and Livestock [MAG] in Paraguay, Ministry of Agriculture, Livestock and Food [MAGA] in Guatemala, and National Service of Agri-Food Health and Quality [SENASA] in Honduras) analyze the information provided by the applicant in the consultation forms and evaluate the nature of the product, most notably whether such products have a novel combination of genetic material or not. If the final organism has a "novel combination of genetic material," it is considered as LMO, and it will fall under the biosafety regulations (Lema, 2019; Whelan & Lema, 2015). This means the nature of the product is an important element for regulation in these seven countries, most notably the definition of "novel combination of genetic material." For example, a "novel combination of genetic material" is explained by domestic regulations of these countries as

- "a stable insertion of one or more genes or DNA sequences that codifies to protein, elements of the RNAi process, double-stranded RNA, and other sequences including information for signal peptides or regulatory sequences," according to Chile (SAG, 2017);
- "a gene, set of genes or DNA sequences that are part of a defined genetic construction and that have been introduced in the genome of an organism on a stable way, by the use of modern biotechnology, overcoming natural physiological barriers of reproduction" for Colombia (Official Journal of Colombia, 2018);
- "a stable insertion in the genome, of one or more genes or DNA sequences that codify: DNA double helix DNA, RNA, proteins or regulatory sequences, that cannot be obtained by conventional breeding or are not found in nature," for both Guatemala and Honduras (Central American Journal of Guatemala, 2019).

In conclusion, if NCAs determine that the final product has a novel combination of genetic material, these will be considered LMOs and regulated as such. Then applicant needs to follow the administrative procedure stated in biosafety legislation of the respective country to receive an authorization for the use of LMOs. If these products are not considered as LMOs, then the application is excluded from the LMO biosafety legislation.

The assessment to determine regulatory status of precision breeding products is complemented by additional considerations based on each country's provisions. For example, in Argentina, the LMO definition uses two complementary criteria: (i) the definition of products of "modern biotechnology" as used in Art. 3 of the CPB and (ii) the definition of "event" in accordance with Resolution 701/2011 (Lusser & Rodriguez, 2012). "An event" is defined by Art. 2 of Resolution 701/2011 as the joint and stable insertion into the plant genome of one or more genes or DNA sequences that are part of a defined genetic construct. And, for Brazil, a product derived from the use of innovative techniques of precision breeding should have at least one of the following characteristics: (1) absence of recombinant nucleic acids, (2) nucleic acids not multiplying in living cells, (3) targeted site mutations with proven absence of recombinant nucleic acids, (4) temporary expression of recombinant nucleic acids, or (5) no permanent modification of the genome (Official Journal of the Federal Government of Brazil, 2018).

Survey response on R&D activities

In terms of R&D on precision breeding techniques, our investigation shows that some universities and research institutions in the majority of these countries develop research activities on products using precision breeding under containment and/or confinement.

3.1.2 | Subgroup II: Countries taking initial steps toward a legal approach to precision breeding

The biosafety legal frameworks of nine countries, namely, Costa Rica, Dominican Republic, Ecuador, El Salvador, Mexico, Nicaragua, Peru, Uruguay, and Venezuela, contain the LMO and modern biotechnology legal definitions of the CPB. These countries reaffirm such definitions by stating equal, or almost equal, meanings into their domestic biosafety legislation and regulations.

Survey results on regulatory matters

Our results show that these nine countries have not adopted any legal provisions related to precision breeding. None of these countries have stated an official declaration regarding under which conditions precision breeding products will fall, or not fall, under domestic regulatory oversight. Initial discussions are currently under development with respect to the regulatory status of precision breeding products in the majority of these countries. For instance, a legal proposal to include certain provisions related to precision breeding into biosafety legislations is currently under development in Ecuador, El Salvador and Peru. Additionally, a new risk regulation for products derived from precision breeding that will not be treated as LMOs is also subject to evaluation in most countries including Costa Rica, Dominican Republic, El Salvador, Mexico, Panama, Peru, and Venezuela. Our investigation shows that Ecuador, Mexico, and Peru affirm that some products derived from precision breeding have to be treated as LMOs according to the CPB and domestic legislation. For instance, these three countries have a common understanding that

some products derived from gene drive systems, RNAi, and synthetic biology could likely be considered as LMOs. Other countries such as Costa Rica, Dominican Republic, Ecuador, and Venezuela have not yet defined whether products derived from precision breeding will be treated as LMOs.

Survey results on R&D activities

Our study shows that a few universities and research institutions among these countries are doing early studies under containment on products using precision breeding techniques.

3.1.3 | Subgroup III: Countries currently drafting biosafety legal frameworks

Twelve Caribbean countries, namely, Antigua and Barbuda, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Saint Lucia, Saint Vincent and the Grenadines, Suriname, The Bahamas, and Trinidad and Tobago, have all made greater efforts towards the preparation and/or revision of biosafety bills for a future enactment (Rosado & Craig, 2017). However, currently, these countries face a de facto moratorium regarding the importation and use of LMOs until they have a biosafety legal framework in place (Rosado & Craig, 2017).

Survey response on regulatory matters

Our results confirm that domestic biosafety legal frameworks in these countries are still under development. Also, up to now, there is no official position from these 12 Caribbean countries on whether products derived from precision breeding will be considered LMOs or not. According to our results and considering that most of these countries are CPB Parties, biosafety bills and proposals of these Caribbean countries will include legal definitions of LMO and modern biotechnology as stipulated in Art. 3 of the CPB. In addition, our investigation shows that some Caribbean countries, such Antigua and Barbuda and Grenada, consider that current biosafety bills should include provisions to determine the regulatory status of products derived from precision breeding. However, the approach to determine such regulatory status is still under evaluation in both countries. Additionally, other Caribbean countries, such as Saint Lucia and Suriname, are initially discussing whether products derived from precision breeding will be considered LMO or not. Also, another topic of discussion related to precision breeding in Caribbean countries, such as Antigua and Barbuda, Grenada, Saint Lucia, and Suriname, is whether or not a new risk regulation for products derived from precision breeding that will not be treated as LMOs shall be included into biosafety bills.

Survey response on R&D activities

Little information was retrieved from these Caribbean countries with respect to R&D activities with precision breeding techniques. It is highly likely that these countries are not carrying out R&D activities with precision breeding nor producing LMOs. In fact, agricultural production in these Caribbean countries is not very large as most countries rely on import of the majority of their agricultural commodities (e.g., maize, soybean, cotton, and canola) from the United States (USDA-FAS, 2020).

3.2 | Second cluster: Countries that do not adopt the CPB's LMO definition

In the LAC region, there are five countries, namely, Bolivia, Cuba, Jamaica, Panama, and Saint Kitts and Nevis, which have enacted biosafety regulations but have not adopted the CPB's LMO definition (Table 3; Figure 1). Instead, these countries have adopted a different legal definition as they regulate GMOs instead of LMOs. For instance, GMO definition in Cuba, Panama, and Saint Kitts and Nevis is fairly similar to the EU's GMO definition. In the EU, the term GMO is defined by Art. 2(2) of Directive 2001/18/EC, which states that a "genetically modified organism (GMO) means an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination" (Official Journal of the European Communities, 2001). It has often been debated whether the process is sufficient (Schauzu, 2013), or a combination of both process and product is needed (Sprink et al., 2016), to determine what is a GMO in the EU. However, a recent analysis of both the wording, the general scheme, and the "spirit" of the EU GMO legislation indicates that both the technique used (process) and the level of novelty of the resulting genetic alteration (product) must be considered (van der Meer et al., 2021), thus making the EU GMO definition largely, though not fully, in agreement with the CPB LMO definition. For the remaining countries, such as Bolivia and Jamaica, the GMO definition is based on a process-based approach.

3.2.1 | Subgroup IV: Countries that define GMO similar to the European Union

The biosafety laws of Cuba, Panama, and Saint Kitts and Nevis regulate GMOs instead of LMOs. Here, these legal instruments state only that the product needs to have a genetic modification that does not occur naturally in order to be considered a GMO. None of the legal frameworks in these countries state that a GMO should possess a "novel combination of genetic material" as stated in Art. 3 of the CPB. In addition, the definition of the techniques used to develop a GMO also varies from the Art. 3 of the CPB. In fact, these legal frameworks do not mention modern biotechnology. Instead, each country has stated its own definition of "genetic engineering" or "gene techniques" that leads to the production of a GMO. They deviate however slightly from the EU GMO definition in that there is no indication of whether a stably inserted or transient introduction of genetic material into the genome of the host organism defines the resulting product/organism as GMO, whereas this is referenced (though not as an

TABLE 3 Survey results: State-of-art of precision breeding in LAC countries of the second cluster (e.g., countries that do not adopt the CPB's LMO definition and, instead, regulate GMOs)

Subgroup	Country	Precision breeding		Biosafety legal framework for GMOs
		Legal provisions	R&D activities	
Subgroup IV: Countries that defines GMOs similar to the European Union	Cuba	Under initial discussions	The Plant Biotechnology Institute (IBP) is doing studies on pulses and fruit and berry crops with the use of genome editing, cis-/intra-genesis, RNAi. Also, The Center for Genetic Engineering and Biotechnology (CIGB) also studies the use of genome editing techniques in pulses. Both IBP and CIGB carry out such research activities under containment and confinement.	Yes, since 1999. Biosafety Decree-Law 190 (Official Gazette of Cuba, 1999).
	Panama	Under initial discussions	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	Yes, since 2002. Biosafety Law 48 (Official Gazette of Panama, 2002)
	Saint Kitts and Nevis	Under initial discussions	No authorization has been made to institutions (governmental or private) to use precision breeding techniques and/or its products.	Yes, since 2012. Biosafety Act 14 (Saint Christopher and Nevis Official Gazette, 2012).
Subgroup V: Countries with a different definition of GMOs	Bolivia	None	NIF	Yes, since 1997. Biosafety Regulation of Supreme Decree No. 24676 (Official Gazette of the Plurinational State of Bolivia, 1997).
	Jamaica	None	NIF	Yes, since 1997. Plants (Importation) Control Regulations under section 38 of The Plants (Quarantine) Act (The Jamaica Gazette, 1997).

Note: Contained use refers to activities in laboratories, glasshouse, and greenhouse, and confined use makes reference to activities in confined field trials.

absolute requirement) in the EU GMO legislation (see Directive 2001/18/EC, Annex IA, part 1).

For instance, Cuba, Panama, and Saint Kitts and Nevis have a common understanding that a GMO is "any living organism in which the genetic material has been modified in a way that does not occur naturally or in a different way than natural." Such definition which recalls Art. 2(2) of the EU Directive 2001/18/EC, it is stated in the domestic legislation of Cuba, Panama, and Saint Kitts and Nevis, specifically in Art. 3 of the Biosafety Decree-Law 190 (Official Gazette of Cuba, 1999), Art. 6 of the Biosafety Law 48 (Official Gazette of Panama, 2002), and Part I of the Biosafety Act 14 (Saint Christopher and Nevis Official Gazette, 2012), respectively. However, none of these domestic instruments make reference to the definition of what is consider natural.

In CUB, the Cuban Biosafety Decree-Law 190 does not define "a different way than natural" nor which kind of technologies are needed to modify an organism and be considered as GMOs. This legislation only states that such modifications should be different from those occurring naturally. In Panama, Biosafety Law 48 indicates a general explanation of what "naturally" means making reference to multiplication and/or natural recombination. In addition, the Panamanian Law 48 states that gene technology refers to "techniques that permit the manipulation of the DNA or RNA, without the need for sexual compatibility of genus or species." Similar to the Panamanian legislation, the Biosafety Act 14 of Saint Kitts and Nevis also defines "in a way that does not occur naturally" as the use of gene technology. Saint Kitts and Nevis's Part I Biosafety Act 14 defines "gene technology" as "techniques that involve the isolation, characterization, modification and introduction of deoxyribonucleic acid into cells or viruses."

Survey results on regulatory matters

Our results show that Cuba, Panama, and Saint Kitts and Nevis have not adopted any legal provision related to precision breeding. None of these countries have stated an official declaration regarding under which conditions precision breeding products will fall, or not fall, under domestic regulatory oversight. Our investigation shows that only Cuba and Panama are probably the countries that most likely will regulate some products derived from precision breeding, at least initially. In fact, both countries affirm that technologies such as genome editing techniques, epigenetic modification, gene drive systems, agroinfiltration, cis-/intra-genesis, grafting, reserve breeding, RNAi, and synthetic biology are likely to generate a GMO and fall under domestic legislation. Saint Kitts and Nevis, on the other hand, is not planning to treat any product derived from precision breeding as GMO.

Survey results on R&D activities

Our results show Cuba is leading studies on different crops using precision breeding techniques in containment in the Caribbean subregion.

3.2.2 | Subgroup V: Countries that apply other definition of GMO

In Bolivia and Jamaica, the definitions of GMO and genetic engineering in accordance with their domestic legislation also differ from the LMO and modern biotechnology definitions of the CPB and from the GMO and modern biotechnology definitions from the EU. Under the GMO definition of these countries, both Bolivia and Jamaica make reference to the use of certain techniques and in the case of Bolivia also to the final product. Similar to Cuba, Panama, and Saint Kitts and Nevis, legal frameworks in Bolivia and Jamaica do not state that a GMO should have a "novel combination of the genetic material" or a stably inserted or transient introduction of genetic material into the genome of the host organism.

In Bolivia, According to Annex I Biosafety Regulation of Supreme Decree No. 24676, a GMO is defined as "any living organism in which the genetic material has been modified through any genetic engineering technique" (Official Gazette of the Plurinational State of Bolivia, 1997). In fact, "genetic engineering" is defined, according to Art. 5 Biosafety Regulation of Supreme Decree No. 24676, as a "process in which a gene from an organism is transferred to another organism by the manipulation of genetic information (genes)." In other words, the regulatory trigger of Bolivia is both the process and the final product. For instance, a product will be classified as GMO if there is a gene transfer between two organisms and if such process is made by any genetic engineering technique. Here, there is no clear definition of manipulation of genetic material nor a differentiation between what is consider natural and which technologies generate a GMO.

Finally, in Jamaica, Part II of Plants (Importation) Control Regulations under section 38 of The Plants (Quarantine) Act defines a "genetically modified plant" as "a plant that has been genetically modified and imported into Jamaica for the purpose of experimentation under controlled conditions" (The Jamaica Gazette, 1997). The Plants (Importation) Control Regulations does not provide further explanation with respect to which genetic engineering procedures are involved to generate a genetically modified plant. Also, the Jamaican regulation does not contain an explanation of what genetic modification means.

Survey response on regulatory matters

Our results show both Bolivia and Jamaica have not adopted any legal provision related to precision breeding nor they have stated a political position regarding under which conditions precision breeding products will fall, or not fall, under domestic regulation.

Survey response on R&D activities

No information was founded in Bolivia and Jamaica regarding R&D activities with precision breeding techniques in these countries.

4 | DISCUSSIONS

4.1 | Definitions: Ambiguity when defining and interpreting scientific terms derived from LMO and GMO legal definitions

The LMO or GMO definition of countries with biosafety legislation, but without any provisions relevant to the regulatory status of precision breeding, requires further legal interpretation of specific terms including "novel combination of genetic material," "manipulation of genetic material," and what is considered "natural." The lack of clarification on the meaning of these terms can provoke ambiguity when applying the biosafety law in products derived from precision breeding (Table 4).

4.1.1 | What is considered to be a novel combination of genetic material?

Countries in subgroup I are currently defining "a novel combination of genetic material" in their respective biosafety regulations as a key criterion to determine the regulatory status of precision breeding products. At this point, there is no consensus about this definition. A novel combination of genetic material is not defined by the CPB. However, Art. 2 of the CBD defines "genetic material" as any material of plant, animal, microbial, or other origin containing functional units of heredity. In other words, genetic material broadly refers to nucleic acids containing genetic information (Rabitz, 2019). Based on the CPB's usage of the term "genetic material," it is suggested that the CPB's references to "novel combination of genetic material" can be understood to refer to a novel combination of nucleic acids containing functional units of heredity (Mackenzie et al., 2003).

A novel combination of such material may refer to a combination of nucleic acids that was not previously known to exist at the time it was first produced (Rabitz, 2019). In fact, such novelty was interpreted by the United Nations Environment Technical Guidelines to refer to organisms that are specifically produced using recombinant DNA and related techniques (Andree, 2007). For instance, a gene editing technique may not produce a novel combination of genetic material as it may only be used to delete or add a nucleotide that is already present in the species population (Everett-Hincks & Henaghan, 2019). Therefore, such explanation can be applicable to interpret the legal meaning of "novel combination of genetic material" in countries of subgroup II and subgroup III that adopted and will adopt the LMO legal definition of the CPB and currently they lack regulations to determine the regulatory status of precision breeding.

4.1.2 | Which precision breeding products does not have a novel combination of genetic material?

Countries categorized in subgroup I have already determined the regulatory status of certain products derived from precision breeding. These countries have concluded that such products will not be treated as LMOs under biosafety legislation if these products do not have a novel combination of genetic material based on the assessment of the respective NCAs. For instance, in Colombia, in 2019, ICA received applications to request the regulatory status of CRISPR-Cas 9-mediated genome edited maize and rice (Colombian Institute of Agriculture and Livestock, 2019). Recently, ICA has agreed that the genome edited rice with broad-spectrum resistance to bacterial blight is not considered a LMO because the final product does not contain foreign DNA material (Agro-Bio, 2020). In

TABLE 4 Genetic alterations and their respective likelihood of occurrence in nature or through conventional breeding

Genetic alterations by:	Likelihood of occurrence in nature	May occur through conventional breeding	Classification of countries		
			Subgroups I, II, and III	Subgroup IV	Subgroup V
Oligonucleotide-directed mutagenesis (ODM)[a]	Very high	Yes	√	√	X
Site-directed nuclease 1 and 2 (SDN1/2)[a]	Very high	Yes	√	√	X
RNA-directed DNA methylation (RdDM)	High-very high	N/A	√	√	X
Agroinfiltration	N/A	N/A	√	√	X
Cis-/intra-genesis	Variable	Yes	√	√/X	X
Grafting with GM material	N/A	N/A	√/X	√/X	√/X
Reverse breeding	N/A	N/A	√	√	X
RNA interference (RNAi)	Very high	N/A	X	X	X
Synthetic biology	Variable	N/A	√/X	√/X	X
Gene drive systems	Very low	N/A	√/X	√/X	X

Note: Each LAC country is analyzed for the likelihood that a product with the respective genetic alterations will be regulated as LMO/GMO. √ = not regulated as LMO/GMO; X = regulated as LMO/GMO; N/A = not applicable.

[a]With respect to non-recombinant directed mutations.

Chile, recently, SAG has authorized the use of low linoleic acid content soybean and high oleic acid content *Camelina sativa* as their conventional counterparts, because both products were developed by directed mutagenesis and do not contain a new combination of genetic material (Eriksson et al., 2019). In Argentina, until June 2018, 12 applications, including 10 applications of genome editing in plants, were evaluated in accordance with the Resolution 173/2015, and the majority were excluded from LMO regulation (Eckerstorfer et al., 2019). Most notably, countries such as Brazil, according to Annex I of the Brazilian Normative Resolution 16, describes examples of techniques such as genome editing techniques including ODM and SDNs, epigenetic modification such as RdDM, agroinfiltration, reverse breeding, RNAi, precocious flowering and seed producing technology that could originate a product that it is not considered an LMO. As a result, products derived from these technologies are excluded from the biosafety legislation in Brazil.

4.1.3 | What does "in a way that does not occur naturally" mean?

The biosafety legislation of countries in subgroup IV makes reference to "natural" when describing the GMO definition. Analyzing the biosafety legislation in these countries, "natural" could make reference to the use of conventional or traditional breeding techniques, such as, for instance, multiplication or natural recombination. There is no internationally agreed definition of traditional breeding, but most authors agree that conventional, traditional, or natural make reference to traditional breeding and selection involving techniques, such as natural selection, cross breeding, protoplast fusion, and chemical- or radiation-induced mutation that modify the genetic material within an organism, but do not introduce genetic information from other organisms in a way that, in fact, many jurisdictions consider unnatural (Kinderlerer, 2008). In that case, "non-natural" techniques could potentially include techniques considered modern biotechnology as described in the CPB, as well as most precision breeding techniques. In fact, this GMO definition resembles to some extent the EU biosafety legislation as stated in Art. 2(2) of the EU Directive 2001/18/EC. However, Annex I A of the European Directive 2001/18/EC provides a further explanation of what it considers natural by listing techniques which are not considered to result in genetic modification, on the condition that they do not involve the use of recombinant nucleic acid molecules or GMOs made by techniques/methods other than mutagenesis and cell fusion (including protoplast fusion) of plant cells of organisms which can exchange genetic material through traditional breeding methods, such as: in vitro fertilization, natural processes such as conjugation, transduction, transformation and polyploidy induction. This additional detailed explanation is not found in the biosafety legislation or subsequent regulations of countries in subgroup IV, as a result this generates some ambiguity to what is considered natural according to these jurisdictions.

4.1.4 | How does the manipulation of genetic material work?

Technically speaking, similar to modern biotechnology and precision breeding techniques, conventional breeding also involves the manipulation of genetic information to a certain degree and many times also the transfer of genetic material between different breeding material (e.g., through crossbreeding). However, it is common to find that biosafety legislation includes some variation of the aspect that the transfer should occur through means that do not occur naturally or through conventional hybridizations of plants in order for the final product to be considered a GMO or LMO. It is not always clear though. For instance, biosafety regulations of countries in subgroup V do not state if gene transfer between the donor and host organisms must overcome natural physiological reproductive or recombinant barriers to be defined as GMO. If a gene from an organism is transferred to another organism through biotechnology, and both donor and receptor organisms are from the same taxonomic family, the final product will likely be classified and regulated as a GMO. As a result, cis-genesis and intra-genesis are highly likely to generate GMOs for countries in subgroup V.

4.2 | Legislation: Practicalities to assess the regulatory status of precision breeding products

In addition to interpret the LMO/GMO definition and related terms, other legislation-based requirements are key to assess the regulatory status of products derived from precision breeding. First, some countries in subgroup I have acknowledged in regulations that some techniques of precision breeding do not produce LMOs which facilitates the processing of queries from applicants. Second, new administrative procedure and forms in biosafety regulatory systems have been adopted to NCAs to handle and assess the regulatory status of precision breeding. And, finally, the rapid adoption of legal provisions on precision breeding is strongly connected to the role of agriculture and biotechnology and national economic and political aspects in the countries.

4.2.1 | Some techniques of precision breeding produce LMOs and others do not

Taking into consideration the LMO definition of the CPB, some techniques of precision breeding can, indeed, generate a product defined as LMO (Table 4). For instance, techniques such as the insertion of recombinant DNA through the SDN-2 or SDN-3 approaches (Eriksson et al., 2019), through conventional RNAi applications based on the use of virus-induced or host-induced gene silencing (Dalakouras et al., 2020), and likely many applications of synthetic biology (Keiper & Atanassova, 2020) produce LMOs as defined in the CPB. In fact, some LAC countries, Chile and Colombia, both following the LMO definition as stated in Art.

3 CPB in domestic legislation, are regulating some products derived from precision breeding which fall under the CPB LMO definition. Specifically, Chile and Colombia consider that an organism, or derived product, from a precision breeding technique is considered a LMO if it has a stably inserted novel combination of genetic material. Other technologies do not generate a LMO according to domestic legislation. Some other countries have established a list of examples of possible technologies exempt from biosafety regulation such as in the Brazilian legal system as stipulated in Annex I of the Brazilian Normative Resolution 16.

4.2.2 | Creating procedures and forms to handle applications to request the regulatory status of precision breeding products

A biosafety regulatory system requires the establishment of an administrative system by the development of procedures and tools for the submission and processing of LMO/GMO applications and the regulatory decision making (Rosado & Craig, 2017). Countries of subgroup I have adopted an additional administrative procedure and forms in their biosafety regulatory systems. Such new mechanism allows applicants to query the NCA about the regulatory status of products derived from precision breeding. In Chile and Paraguay, applicants are required to fill a consultation form with information of the precision breeding product about the parental organism, technique, molecular biology, phenotype and prior authorizations in other countries. Once the application is presented to the respective NCA, the NCA will check for completeness according to regulations and, if needed, will contact the applicant to request additional information. After that, the NCA, with the support of the Biosafety Advisory Committee, will assess the application and determine whether products derived from precision breeding will be considered a LMO, and follow biosafety law, or not. For some jurisdictions like Argentina and Colombia, such assessment cannot exceed more than 60 business days. Countries that have biosafety legislation but lack provisions relevant to precision breeding, most notably countries in subgroups II, III, IV, and V, require to adopt similar additional administrative procedures and forms in their biosafety regulatory systems to handle queries to the regulatory status of precision breeding.

4.2.3 | Adopting biosafety legislation is strongly connected to domestic economic and political perspectives related to the role of biotechnology in the countries

Our results show that most R&D activities with precision breeding are carried out in countries that have adopted legal provisions relevant to precision breeding (subgroup I). In fact, the majority of these countries are major exporters of agricultural products, and this may be a contributing factor to their advanced level of legislation in relation to biotechnology and biosafety. For instance, Argentina and Brazil have established a trade related LMO biosafety legal framework and lead the global production of GM soy bean and maize (Smith & Katovich, 2017). Additionally, both countries have sufficient research infrastructure to develop GM crop varieties that not only meet the needs of its farmers but also support a strong economy in the production and trade of commodities (Sasson & Malpica, 2018). Clearly, the economic importance of the agricultural sector and the role of biotechnology in the respective countries are fundamental triggers for the rapid adoption of biosafety law and regulations. As such, it seems that countries leading in LMO cultivation are the same countries that are quickly adapting their biosafety legislation to accommodate gene-edited products thereby supporting the domestic agricultural sector (Turnbull et al., 2021). This is the case of LAC countries such as Argentina, Brazil, Chile, Colombia, and Paraguay that have adopted a harmonized approach to regulate LMOs and to assess the regulatory status of precision breeding products.

The situation may be different in some other countries like in the Caribbean subregion or in other South American countries, which have a small-scale production of agricultural commodities for export purposes and domestic consumption. For instance, most Caribbean countries rely mostly on imports of agricultural commodities (USDA-FAS, 2020), and tourism plays a bigger role in their economy rather than agriculture. This could probably explain why the majority of Caribbean countries still lack biosafety law and few R&D activities have been reported. South American countries such as Bolivia, Ecuador, Peru, and Venezuela have adopted restrictive biosafety legislation and policies to prohibit, inter alia, the commercialization of LMOs in their territories (Rosado & Craig, 2017). In fact, such political measures can minimize the need to adopt legal provisions to determine the regulatory status of precision breeding products in these countries. Further studies are needed to show the potential causal links between regulatory approach, level of R&D activities and political and economic aspects in the targeting countries.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

AR planned and designed the manuscript. AR and DE contributed equally in writing the introduction, country descriptions, and analysis of legal material, discussions, and for assembling and formatting all text material.

DATA AVAILABILITY STATEMENT

The data that support the finding of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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