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The future of agricultural biosafety regulations

Edited by
Clara Rubinstein, Monica Garcia-Alonso, Carmen Vicien and Stuart Smyth

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The future of agricultural biosafety regulations

Topic editors

Clara Rubinstein — Institute for Scientific Cooperation in Environment and Health (ICCAS), Argentina

Monica Garcia-Alonso — Estel Consult Ltd, United Kingdom

Carmen Vicien — University of Buenos Aires, Argentina

Stuart Smyth — University of Saskatchewan, Canada

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Table of contents

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Stephen Allen Morse,
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*CORRESPONDENCE
Clara Rubinstein,
cprubi@gmail.com

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Editorial: The future of agricultural biosafety regulations

Monica Garcia-Alonso[1], Clara Rubinstein[2]*, Stuart J. Smyth[3] and Carmen Vicien[2,4]

[1]Estel Consult Ltd., Berkshire, United Kingdom, [2]Institute for Scientific Cooperation in Environment and Health (ICCAS), Buenos Aires, Argentina, [3]University of Saskatchewan Saskatoon, Saskatoon, Canada, [4]School of Agronomy, University of Buenos Aires, Buenos Aires, Argentina

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Editorial on the Research Topic
The future of agricultural biosafety regulations

Introduction

Progressive and adaptive criteria for biosafety assessments require a collaborative effort across disciplines, experts and institutions around the globe to enable fit-for-purpose, risk appropriate regulations that promote the safe implementation of bio-innovations and their accessibility to society. A number of recent reports provide insights, recommendations, and actions in this direction (OECD, 2024; OECD, 2025; NESTA Report, 2019; Regulatory Horizons Council report, 2022). This is especially relevant, as food systems will have to sustain food security by producing greater yields per area, meet demands to be sustainable, and at the same time produce innovative, affordable foods.

Revisiting the scientific rationale for assessing gene technologies in the light of current knowledge and experience is critical for technologies to advance. Therefore, it was considered timely to compile a set of publications to provide an overview of the current challenges and opportunities for adapting biosafety considerations to support innovative biotechnological applications. This Research Topic features 12 publications authored by over 60 experts, representing realities and views from different world regions and sectors.

Experiences and challenges in developing countries

Experts from Latin American and African countries share experiences and discuss regulatory frameworks, risk assessment approaches and innovative technologies, highlighting regulatory diplomacy and collaboration as enablers of functional and progressive frameworks.

In *"Experiences, learnings and perspectives in the regulation of agricultural biotechnology: the view from Argentina"*, Lewi et al. share their experiences with the revision process carried out between 2020 and 2023, based on the latest scientific knowledge. Collaborative initiatives and outreach actions implemented at the

international level are also described, which resulted in the adoption of Argentina´s criteria for New Breeding Techniques in other geographies. This article stresses that continuous updating and training of risk assessors and inter-agency collaborations are key to enable adaptive frameworks and anticipate future challenges.

In "*Africa and zero hunger agenda: genome editing policy landscape, challenges and opportunities*", Akinbo et al. comment on the historical opposing forces between the need to incorporate technology to ensure food security and strong positions against biotechnology as the main obstacle for adoption. They also review policies in five African countries regarding genome editing and continental initiatives that can promote agricultural innovations in the region.

Complementing this analysis, research conducted in African countries is presented by Rabuma et al., focused on the biosafety regulatory frameworks for genome editing and gene drive technologies. This study provides updated data that can be used to identify and address common challenges to develop effective regulatory frameworks going forward.

An additional complexity is addressed by Fernandez Rios et al., discussing the challenges and global trade implications of genome editing divergent regulatory criteria between regions. The article calls for more harmonized approaches that can not only facilitate trade but also stimulate the use of genome editing to address food security and mitigate climate change effects.

There is a need for adaptive criteria and new models for regulatory oversight

Experts from different sectors offer their views on current regulatory models and propose advancements based on scientific knowledge and experience with risk assessment of gene technologies. Innovative applications in fruits and microorganisms are also discussed as cases that need adaptive criteria to advance.

In *"Naturally transgenic plants and the need to rethink regulatory triggers in biotechnology"*, Fernandez Rios et al. revisit the product vs. process regulatory approach for gene technologies, considering the complexity of plant genetics and the existence of naturally occurring transgenic plants, of which there is growing evidence. This article proposes to rethink the regulatory triggers for plant products derived from gene technologies, in particular, transgenesis.

Along these lines, two articles focus on GM microbial based biologicals. In the first, Karberg reviews the complexities of the microbial world, as the natural genetic exchange among microorganisms shows that natural transgenesis is common, making it difficult to label a microorganism as GM (or not). The article puts into question the scientific relevance of such labels for risk assessments and advocates for a more effective and science-based regulatory approach focused on the microorganisms' actual functions.

In the second, Rubinstein et al. elaborate further on these arguments in *"Genetically modified microorganisms for agricultural use: an opportunity for the advancement of risk assessment criteria in Argentina"*. The article reflects a discussion conducted in Argentina, proposing a change in the current paradigm developed over 30 years ago for transgenic plants. The rationale is based on extensive scientific evidence and concludes that there is a need to adapt regulatory criteria to the microbial world.

Fruit improvement through gene technologies, is exemplified by Klocko in "*Apple improvement, traditional approaches, biotechnology options, and regulatory considerations*". This work describes multiple apple breeding approaches with focus on transgenesis. As global biosafety regulations continue to develop and change, the article points to the need to develop guidelines for these cases, both for the cultivation and for import of engineered fruits, in this case, apple trees and apple derived products.

On regulatory frameworks and the importance of perception

On the regulatory model side, Koch et al. offer the views of experienced developers of GM plants, pointing the 30 plus years of experience with risk assessment in many countries and calling to capitalize on this experience to avoid redundancy in country by country safety reviews of the same cases. The article proposes a global collaborative, harmonized model for risk assessment that is nimble and forward-looking, to keep up with the pace of innovations and enable broader access to their benefits.

Buchman and Kovak offer a US-focused analysis in *"A Call for Congressional Action: Revisiting the U.S. Coordinated Framework for the Regulation of Biotechnology"*. This Policy Brief examines the Coordinated Framework for the Regulation of Biotechnology developed almost 40 years ago and calls for substantial changes for current and future products. Recommendations ask, among others, for the creation of a centralized application submission portal, a horizon scanning for future products of biotechnology and streamlined regulations for familiar products.

On the other side of the Atlantic, Garcia Alonso et al. review the situation of GM crops in the EU, providing an historic framework and discussing the challenges posed by the current regulatory approach. The impacts of the rigid and outdated regulatory oversight of GMOs on innovation, EU farmers access to biotechnology technologies, trade implications and market concentration are discussed. Authors advocate for changes that can reduce the current complexity and unpredictability of the process, aligning the regulatory oversight of GM crops with current scientific knowledge and international practices.

Finally, in *"Agricultural biotechnology in the courts: judicial opinions and commentary"*, Kershen provides a thorough analysis of judicial opinions in different countries and their impacts on innovation and access to the benefits of biotechnology by society. The influence of public perception on decision makers and judicial decisions and the consequences for agricultural development are also discussed.

In summary, this Research Topic presents relevant perspectives and diverse international views on the necessary changes to support and advance innovation. These contributions provide scientific arguments emphasizing the importance of ensuring that agricultural biosafety regulations are fit for purpose, internationally harmonized - where possible- and forward looking, grounded on science and risk assessment. Regardless of geographical regions, this Research Topic shows the common challenges faced, the consensus on the need for a paradigm shift

and the critical role of regulatory diplomacy in preparing for the future.

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EDITED BY
Clara Rubinstein,
Institute for Scientific Cooperation in Environment and Health (ICCAS), Argentina

REVIEWED BY
Dalia Marcela Lewi,
Ministerio de Agricultura, Argentina
Karen Hokanson,
Agriculture and Food Systems Institute, United States

*CORRESPONDENCE
Wendy Craig,
craig@icgeb.org
Tilahun Rabuma,
tilefire@gmail.com

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Navigating biosafety regulatory frameworks for genetic engineering in Africa: a focus on genome editing and gene drive technologies

Tilahun Rabuma[1,2]*, Felix Moronta-Barrios[2] and Wendy Craig[2]*

[1]Department of Biotechnology, College of Natural and Computational Science, Wolkite University, Wolkite, Ethiopia, [2]Regulatory Science Group, International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

Genome editing and gene drive technologies are increasingly gaining attraction in Africa, with researchers exploring their potential applications in agriculture, health and the environment. Acknowledging that robust regulatory frameworks are crucial in facilitating the development and utilization of these technologies, informed decision-making is, however, being impeded by the fragmented information availability and readiness of regulatory authorities on the continent.

Objectives: This study investigates the regulatory frameworks governing genome editing and gene drive technologies in African countries, identifies common regulatory challenges and proposes actionable solutions.

Methods: Primary data were collected through questionnaires and complemented by analysing existing biosafety regulations from online databases and scientific literature.

Results: Our findings suggest that while a few African countries have recently updated their regulatory frameworks, many are still under discussion. Challenges to development and implementation include limited resources, expertise, awareness, and public resistance.

Conclusion: The findings underscore the urgent need for further development in regulatory capacities. By shedding light on these challenges, our study could provide African regulators with valuable insights to guide the formulation of effective regulatory frameworks. Such frameworks are essential for harnessing the potential of genome editing and gene drive technologies while safeguarding human health and the environment in Africa.

KEYWORDS

biosafety regulations, emerging biotechnologies, regulatory frameworks, Africa, genome editing, gene drive

1 Introduction

Genome editing is the ability to make precise changes to DNA sequences within organisms using engineered nuclease enzymes to cut and replace existing DNA segments (Fridovich-Keil, 2024). Among the numerous genome-editing methods now available, CRISPR/Cas-based genome editing stands out as the most convenient, efficient, precise and

widely used genome editing tool (Knott and Doudna, 2018; Li et al., 2022; Matsumoto and Nomura, 2023). Furthermore, CRISPR/Cas-based gene drive systems enable the manipulation of self-propagating genetic elements, which are passed on to offspring at frequencies surpassing Mendelian inheritance (Bier, 2022). Thus, gene drives bias inheritance patterns by increasing their prevalence in successive generations (Alphey et al., 2020).

In Africa, genome editing and gene drive technologies hold promise for addressing pressing challenges in agriculture, health and the environment. For instance, the increasing food demand, exacerbated by factors such as climate change, diseases, and limited access to fertilizers and agrochemicals, necessitates innovative solutions. Genome editing technology is another approach that offers avenues to enhance agricultural productivity by, for instance, developing drought tolerance (Osakabe et al., 2016; Sami et al., 2021; Shelake et al., 2022), disease resistance (Karmakar et al., 2022), salt tolerance (Saradadevi et al., 2021; Shelake et al., 2022), and nutritional improvement (Ku and Ha, 2020; Nagamine and Ezura, 2022).

Likewise, the escalating prevalence of insect-borne diseases like malaria in tropical and subtropical regions of Africa underscores the urgency of novel public health interventions. Despite various control strategies, African countries continue to grapple with the highest malaria burden globally (Ombogo, 2023). In pursuit of the ambitious goal of malaria elimination by 2030, the World Health Organization (WHO) has prioritized gene drive mosquitoes as a transformative technology (Wamba, 2023), which represents a promising new tool for the elimination of malaria and other mosquito-borne diseases (North et al., 2020; Metchanun et al., 2022).

Researchers are increasingly drawn to gene drive technologies due to their potential as highly effective, cost-efficient, and enduring solutions (Bier, 2022; James et al., 2018; James et al., 2023). However, the adoption of genome editing and gene drive technologies highly depends on government regulation in each country (Jenkins et al., 2021). Such regulation plays a crucial role in determining whether approval is necessary and thus given for the development and commercialization of these products (Entine et al., 2021). Moreover, regulatory frameworks serve to safeguard human health and the environment while fostering public trust and legal certainty for research institutions and industries (Zawedde et al., 2018; DiversityS. O. T. C. O. B., 2000).

The global regulatory landscape for genome-edited products is evolving rapidly (Tripathi et al., 2022). While some countries have swiftly adapted legislation or regulatory frameworks to support genome editing, others remain in the policy formulation stages (Jenkins et al., 2021), and some still classify these products as Genetically Modified Organisms (GMOs) (Hundleby and Harwood, 2022). Whether genome-edited products are exempt from GMO regulations often depends on the specific genome-editing techniques used. For instance, certain gene editing methods, such as site-directed nucleases (SDNs), including SDN-1, which induces gene disruptions through insertions or deletions, and SDN-2, which uses homologous templates for gene correction or modification, are fully exempted in some countries (Wolt et al., 2015). In contrast, SDN-3, which involves inserting larger DNA elements or foreign genes, is typically treated as a GMO (Vora et al., 2023). Countries like Argentina, Australia, Brazil, Chile, India, Kenya, Nigeria, Paraguay, Russia, and the USA have exempted genome-edited plants from GMO regulations, while China and the UK follow simplified GMO regulations. The EU, New Zealand and South Africa, however, regulate genome-edited products as GMOs, and in many countries, proper regulations or discussions are still lacking (Friedrichs et al., 2019; Schmidt et al., 2020; Vora et al., 2023).

Although regulatory frameworks for GMOs have been established in many African countries following their adoption of the Cartagena Protocol on Biosafety (Akinbo et al., 2021; Quemada, 2022), several countries are still working to effectively manage modern biotechnology and implement national biosafety frameworks for GMOs (Komen et al., 2020). Furthermore, most African countries do not have adequate regulatory frameworks specifically tailored to regulate genome editing and gene drive technologies regulatory oversight (Masehela and Barros, 2023). A well-established GMO regulatory framework can be a logical departure point when contemplating genome-editing governance (Abkallo et al., 2024). In this regard, efforts have been made to incorporate genome editing products into the existing GMO biosafety regulatory frameworks on a case-by-case basis; however, concerns remain about the overly restrictive nature of regulations concerning the introduction and development of genome editing and gene drive products in Africa (Ongu et al., 2023). Additionally, existing laboratory biosafety and biosecurity review processes may not effectively address the unique challenges posed by gene drive research and its components (Millett et al., 2022). Uncertainties such as limited access to laboratories, equipment and reagents, a shortage of trained professionals for molecular biology work, and a low rate of returnees among the trained professionals working internationally have significantly negatively impacted genome editing research and development in Africa (Abkallo et al., 2024), which, in turn, has also affected the development of regulatory frameworks for genome editing and gene drive technologies.

Concerns also arise regarding the potential dispersion and persistence of gene drive transgenes beyond the release area, posing challenges to their regulation under existing GMO regulatory frameworks (Gene Drives on the Horizon, 2016; Programme, 2021). Furthermore, the lack of mitigation and traceability strategies (Noble et al., 2018), together with limited experience in risk assessment, exacerbates regulatory uncertainties (AGBC, 2022). Responsible field-based gene drive research also raises significant concerns (Thizy et al., 2020), further complicating regulatory efforts. As a result, the regulatory status of genome editing and gene drive technologies in Africa remains uncertain, raising questions about the adequacy of existing frameworks and the need for new or updated regulatory frameworks (Asquer and Morrison, 2022). However, a few African countries have initiated efforts to incorporate genome editing products into their biosafety regulatory frameworks, such as Nigeria and Kenya (Boluwade and Smith, 2021; Tripathi et al., 2022), while other African countries like Burkina Faso, Mali and Uganda plan to start field trials of gene drive mosquitoes within the next 5–10 years (Hartley et al., 2021).

Given these challenges, an African Union policy consultation advocates for a more enabling and science-based regulatory approach in order to leverage genome editing and gene drive technologies (Komen et al., 2020). Dolezel et al. (2020) suggested a need for a comprehensive examination of current GMO regulatory frameworks to determine their suitability for addressing the

potential risks and challenges posed by gene drive applications. A comprehensive analysis is required to shed light on the existing regulatory frameworks that govern these technologies in African countries. The aim of our study was, therefore, to analyze the status of regulatory frameworks for genome editing and gene drive technologies and identify gaps in their development and implementation in African nations. To this end, the regulatory approaches of various African countries were compared and contrasted, common trends and differences were identified, the adaptability of the current regulatory frameworks to emerging technologies was assessed and recommendations for improving biosafety regulations in African countries were formulated.

This serves as a comprehensive update on the current status and challenges facing biosafety regulatory frameworks in African countries concerning genome-edited and gene drive technologies, contributing to the advancement of these technologies on the continent. This information can equip African regulators, policymakers and researchers with valuable insights into the establishment of robust regulatory frameworks for genome editing and gene drive products.

2 Methodology

This exploratory study adopted a qualitative approach to investigate the regulatory environment for genome editing and gene drive technologies in Africa. A survey was designed with five distinct sections, combining both closed-ended and open-ended questions, thereby allowing for in-depth insights into the aspects of biosafety regulations. The survey was deployed between 22 July and 07 August 2023. The initial section gathered demographic information and general insights. Subsequently, the survey enquired into core aspects, including the status of biosafety regulatory frameworks for genome editing and gene drive technologies, international collaborations and harmonization efforts, identified gaps and challenges in existing regulations and explored public perceptions along with ethical considerations. The survey targeted Cartagena Protocol national focal points and national competent authorities across 54 African countries, aiming to discern the presence and effectiveness of regulatory frameworks. Additionally, data on national biosafety regulatory status was cross-verified through the database of Biosafety Clearing-House (BCH) and the one curated by the African Biosafety Network of Expertise (ABNE). To enhance the comprehensiveness of our findings, a literature search was conducted to supplement and triangulate the information gathered from the questionnaire and databases, ensuring a robust and multifaceted analysis of the regulatory landscape in Africa.

3 Results

3.1 The authorization for genetic engineering applications in agriculture

The survey findings reveal varying degrees of authorization for genetic engineering applications across African countries at different developmental stages. For example, some African countries may have authorized only research and development (R&D) and confined field trials (CFTS) activities, as exhibited in DRC, Tunisia and Uganda, while others may have authorized GM crops, including the importation and cultivation for feed and food applications (Table 1). Notably, Eswatini, Kenya and Nigeria have authorized genetic engineering applications at nearly all developmental stages. In contrast, countries such as Ethiopia, Ghana, Mozambique, Uganda and Zambia have limited their authorization to laboratory research and confined field trials. While in countries such as Benin, Côte d'Ivoire, DRC, Gambia, Mali, Nambia, Senegal, Togo, Tunisia and Zimbabwe, authorizations for genetic engineering applications at various stages of development are still lagging compared to other African countries.

3.2 Status of regulatory framework for genome editing and gene drive technologies in Africa

According to survey respondents, Benin, Eswatini, Kenya, Nigeria and Uganda have established suitable regulatory frameworks to regulate genome editing and gene drive technologies and their products. In Benin, Eswatini and Uganda, existing biosafety regulations can be applied to regulate genome-edited and gene drive products. Kenya and Nigeria have implemented specific regulations tailored to oversee these technologies. In this sense, Nigeria has amended existing biosafety regulations to encompass genome editing products within governmental safety review and approval procedures. Kenya has also developed a new genome editing-specific regulatory framework that oversees technology use within the safety review and requisite governmental approval. For gene drive technology, the Kenyan respondents replied that existing biosafety regulations would be applied. Survey results further highlight that Eswatini, Nigeria and Uganda adopt a process-based approach to regulating these technologies, while Benin and Kenya employ a product-based approach to regulating genome editing technology (Table 2). In Zambia, on the other hand, the approach to regulation remains under development.

Regarding genome editing techniques, responses from Benin, Kenya, Nigeria and Uganda indicate that those techniques incorporating site-directed nucleases-3 (SDN-3) fall under regulatory oversight, while those utilising site-directed nucleases-1 (SDN-1), site-directed nucleases 2 (SDN-2) and Oligonucleotide-directed mutagenesis (ODM) are exempted from existing regulation oversight on a case-by-case basis (Table 2; Figure 1). Additionally, respondents from Eswatini indicated that SDN-1, SDN-2 and SDN-3(with *cis-insert*) are exempted from GMO regulations on a case-by-case approach, while SDN-3 (with *trans-insert*) are regulated under existing GMO regulations. Similarly, in Zambia, in which the regulatory framework is under development, SDN-2 and SDN-3 categories are expected to fall under existing regulations, while SDN-1 and ODM will be deregulated from GMO regulation on a case-by-case basis.

TABLE 1 The status of authorization for biotechnology applications in African countries according to the survey respondents. Data was collected between 22 July and 07 August 2023.

Countries	R&D[a]	CFT[b]	Open-field trial[c]	Pre-market authorization[d]	Importation[e]		Cultivation[f]	
					Feed	Food	Feed	Food
Benin	–	–	–	–	–	–	–	–
Cote d'Ivoire	–	–	–	–	–	–	–	–
DRC	+	–	–	–	–	–	–	–
Eswatini	+	+	–	+	+	+	+	+
Ethiopia	+	+	+	–	–	–	–	–
Gambia	–	–	–	–	–	–	–	–
Ghana	+	+	+	+	+	+	0	0
Kenya	+	+	–	+	+	+	+	+
Mali	–	–	–	–	–	–	–	–
Mozambique	+	+	–	–	–	–	–	–
Namibia	–	-	–	–	–	–	–	–
Niger	–	-	–	–	–	–	–	–
Nigeria	+	+	–	+	+	+	+	+
Senegal	–	–	–	–	–	–	–	–
Togo	–	–	–	–	–	–	–	–
Tunisia	+	–	–	–	–	–	–	–
Uganda	+	+	–	–	–	–	–	–
Zambia	+	+	–	–	+	+	–	–
Zimbabwe	–	–	–	–	–	–	–	–

(Mark +: denotes yes; -: denotes "No", 0: denotes no response given).
[a]Research and Development (R&D): The early-stage activities involving laboratory and greenhouse experiments aimed at investigating the potential and safety of genetic engineering technologies.
[b]Confined Field Trials (CFTs): Small-scale, controlled experiments in open environments to assess genetically engineered crops while preventing their establishment and spread.
[c]Open Field Trials: Larger-scale controlled releases of genetically engineered crops into the environment to evaluate their performance under real-world conditions, collect data, and mitigate adverse effects.
[d]Pre-Market Authorization: The approval process required before genetically engineered crops can be sold or distributed commercially, ensuring they meet safety and regulatory standards.
[e]Importation: The authorization to bring genetically engineered crops or products containing genetically engineered materials into a country for research, trials, or commercial purposes.
[f]Cultivation: The stage where genetically engineered crops are grown on a commercial scale following successful authorization for general agricultural use.

3.3 Challenges

3.3.1 Identified gaps in the implementation of regulatory frameworks

Respondents highlighted significant challenges in the implementation of national biosafety regulations for genome editing and gene drives across most African countries. Top among these challenges are limited resources and expertise, coupled with a lack of awareness or understanding of the technologies (Figure 2A). Additionally, the implementation of these regulations faces hurdles in certain countries due to public resistance or scepticism. Notably, respondents from The Gambia and the Democratic Republic of Congo (DRC) indicated gaps in their regulatory framework, with the DRC notably lacking a biosafety law for these technologies. The response from Benin underscores that although lack of awareness or understanding, limited resources and expertise, and public resistance or scepticism exist as gaps in the implementation of the national legal framework for genome editing and gene drive technologies, the issues are so dynamic and difficult to address, suggesting the need for a holistic, comprehensive approach to implementing the framework.

3.3.2 The major challenges in harmonizing biosafety regulatory framework in African countries

The survey findings indicate significant obstacles to aligning the biosafety regulatory framework for genome editing and gene drive technology at a regional or international level in African countries. Foremost among these harmonization challenges is the lack of coordination and information sharing between regulatory authorities. Additionally, differing concerns about technology transfer and intellectual property rights, as well as variations in regulatory frameworks and definitions among African countries,

TABLE 2 Details status of the regulatory framework for genome editing and gene drive technologies in six African countries.

African countries	Does the country have an approved and published regulatory framework?	Types of genome editing technique				Regulatory framework developed and applied	Regulatory approach triggering regulations	Year of approval and publication of biosafety regulatory framework
		SDN-1	SDN-2	SDN-3	ODM			
Benin	–	Deregulated on a case-by-case basis	Deregulated on a case-by-case basis	Regulated	Deregulated on a case-by-case basis	Existing regulation	Product-based	• Not published • Under discussion
Eswatini	–	Deregulated on a case-by-case basis	Deregulated	Regulated	Deregulated	Existing regulation	Process-based	• Not yet published • Under discussion
Kenya	+	Deregulated on a case-by-case basis	Deregulated on a case-by-case basis	Regulated	Deregulated on a case-by-case basis	New guidelines developed	Product-based	Published in 2022
Nigeria	+	Deregulated on a case-by-case basis	Deregulated on a case-by-case basis	Regulated	Reregulated on a case-by-case basis	Modified pre-existing regulations	Process-based	Published in 2019
Uganda	–	Deregulated on a case-by-case basis	Deregulated on a case-by-case basis	Regulated	Deregulated on a case-by-case basis	Existing regulation	Process-based	Under discussion
Zambia	–	Deregulated on a case-by-case basis (under development)	Regulated on a case-by-case basis	Regulated on a case-by-case basis	Regulated on a case-by-case basis	Under discussion	Under discussion	Under discussion

(Mark +: denotes yes; -: denotes "No").

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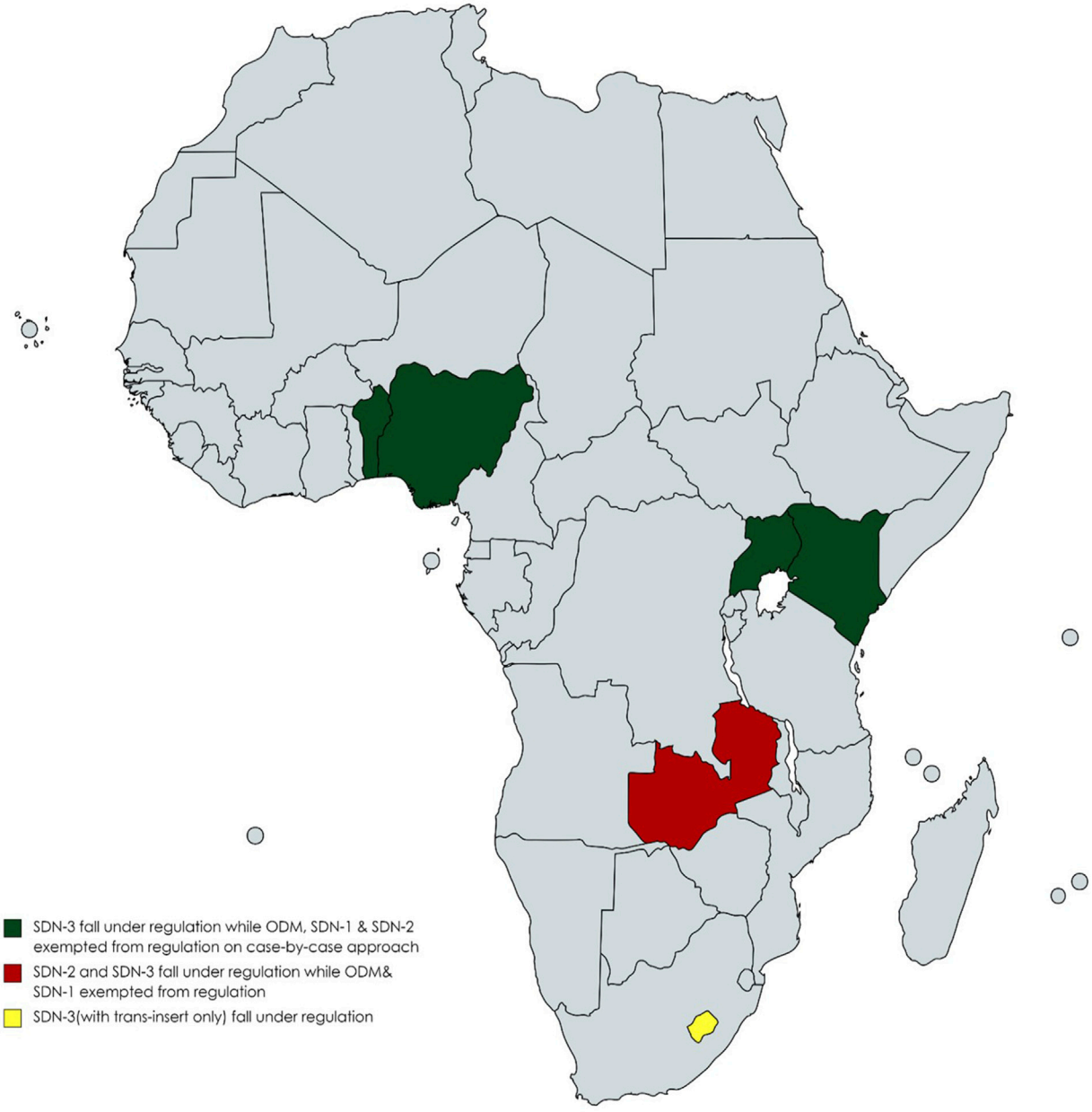

FIGURE 1
Regulation of genome edited products according to the genome editing technique used by country.

pose considerable hurdles. Aligning diverse cultural, social and ethical perspectives also presents challenges. However, respondents identified this as the least significant barrier to harmonizing the biosafety regulatory frameworks (Figure 2B). Thus, unharmonized regulatory frameworks could potentially hinder the application of genome editing and gene derive technologies and future international trade.

3.3.3 Strengthening regulatory frameworks for genome editing and gene drive technologies

This investigation, drawing input from African biosafety authorities, experts, scientists and civil society, underscores several crucial actions necessary for the development and enhancement of biosafety regulatory frameworks for genome editing and gene drive technologies and products (Figure 2C). Foremost among these actions is the investment in training programmes and workshops aimed at regulators and stakeholders. Furthermore, the analysis identified pivotal actions such as the establishment of partnerships with academic institutions for research and capacity building, along with increasing knowledge-sharing with international organizations and experts. Additionally, strengthening collaboration among African countries and the development of specific, standardized risk assessment methodologies for genome editing and gene drive was indicated as an additional crucial action.

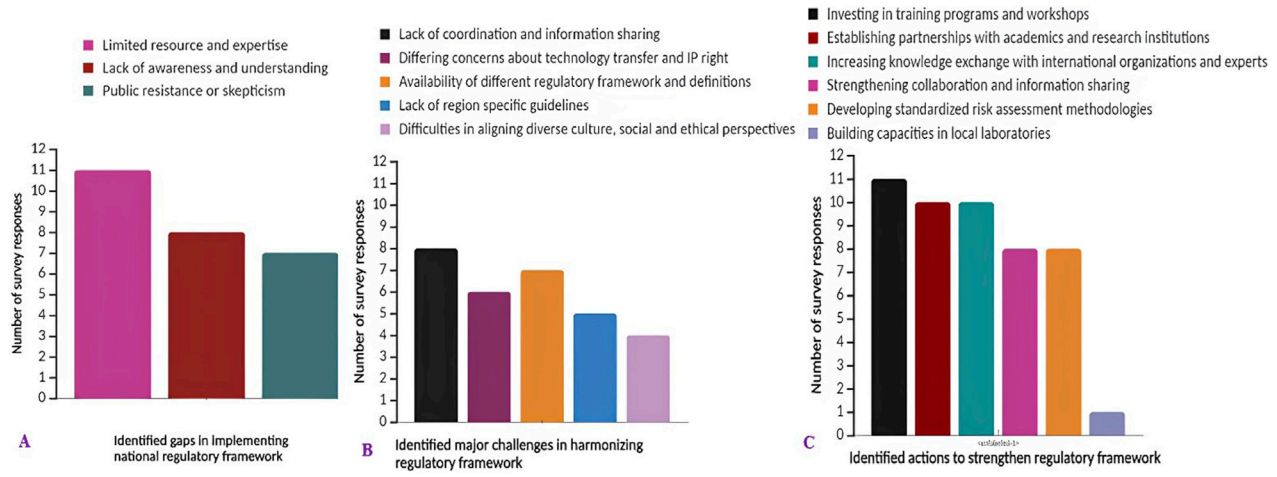

FIGURE 2
The survey response analysis on: **(A)** identified gaps in the implementation of the national biosafety regulatory framework; **(B)** major challenges or barriers in harmonizing biosafety regulations for genome editing at a regional or international level; **(C)** action needs to strengthen the biosafety regulatory framework for genome editing and gene drive technologies.

3.3.4 Public perception, resistance and ethical issues

Responses from nine countries, including Benin, the DRC, Ethiopia, Kenya, Mozambique, Nigeria, Tunisia, Uganda, and Zambia, underline significant public resistance and controversies surrounding genome editing and gene drive technologies and products. The reasons cited for this opposition relate to the early stage of development of these technologies and public concerns regarding potential harm to human health and the environment (Table 3). Moreover, respondents from five countries indicated concerns about the potential for unintended consequences or misuse of these technologies. Social media activism emerged as a key driver of resistance and controversies against these technologies. Notably, respondents from Eswatini reported no controversy or public opposition to genome editing or gene drive, while in Nigeria, although controversies exist, there is no apparent public resistance raised through social media activism to prevent activities with the technologies.

3.3.5 Improving public perception and attitude

Survey responses indicate that public perception can be improved by involving the public more in the decision-making process regarding the release of genome-edited and gene drive products (Figure 3A). Furthermore, providing unbiased information and easily understandable information about these technologies to non-specialists is seen as crucial for improving public perception. Only a few countries mentioned the importance of identifying and defining ethical issues, increasing public confidence in the regulatory systems, and requiring informed consent from recipient communities to support the improvement of public perceptions and attitudes towards genome editing and gene drive technologies.

3.3.6 Ensuring public engagement and transparency

This investigation highlights the importance of public consultation and hearings in the decision-making process regarding genome editing and gene drive technologies (Figure 3B). Additionally, ensuring accessible information about these technologies and proactive stakeholder engagement and transparency in the decision-making process are seen as essential for improving public perception.

3.4 Prospective toward developing/drafting the biosafety regulatory framework in African countries

The current findings highlight the growing interest among several African countries in developing and implementing regulatory frameworks to regulate the use of genome editing and gene drive technologies (Table 4). This includes the formulation of regulatory frameworks aimed at ensuring the safe and ethical use of these technologies within respective national contexts. In countries like the DRC, Eswatini, Ethiopia, Mozambique and Uganda, discussions and drafting efforts are underway to establish modern biosafety regulatory regimes. These countries recognize the need for a regulatory system tailored to address the specific challenges and opportunities presented by these technologies.

3.5 Literature search

3.5.1 Status approval of genetic engineering applications

The scientific literature provides insights into the heterogeneous landscape of approval processes for genetic engineering applications across African countries. While some nations have established regulatory frameworks for authorizing GMOs, including for research and development, CFTs, open field trials activities, and importing for the direct use of GM products, others are still in the developmental stages of such frameworks (Table 5).

10.3389/fbioe.2024.1483279

TABLE 3 Survey analysis on the types of public resistance against genome editing and gene drive technologies.

Countries	Justification for controversies			No controversies about technologies	Is public resistance raised against Genome editing and Gene drive?	Ways of Triggering Public Resistance
	Technologies are early in their development, and thus not enough is known about them	Public believes that products are bad for health	Technologies have the potential to cause unwanted consequences and/or abuse			
Benin	–	–	–	–	+	Social media activism seeks to prevent activities with the technologies
DRC	+	–	+	–	–	–
Eswatini	–	–	–	+	–	–
Ethiopia	+	+	+	–	+	Social media activism seeks to prevent activities with the technologies
Gambia	0	0	0	0	0	0
Kenya	+	–	–	–	+	Social media activism seeks to prevent activities with the technologies
Mozambique	+	+	–	–	0	0
Nigeria	+	+		–	–	0
Tunisia	–	–	+	–	0	0
Uganda	+	–	+	–	+	Social media activism seeks to prevent activities with the technologies
Zambia	–	+	–	–	+	Social media activism seeks to prevent activities with the technologies

(Mark +: denotes yes; -: denotes "No", 0: denotes no response given).

3.5.2 The literature finding on the regulatory landscape of genome editing and gene drive in Africa

Literature findings concerning the regulatory frameworks surrounding genome editing and gene drives in African countries are critical for understanding the various laws, policies and guidelines governing these technologies on the continent. Recent studies have shed light on how different African countries approach genome editing and gene drive regulation. African countries have developed various types of regulatory approvals for genome-edited product usage, i.e., laboratory research and development, confined/small scale field trials, open scale field releases, and multiplication field trials for agronomic performance evaluation and commercialization in African countries (Table 6).

4 Discussion

In light of the diverse regulatory landscapes, approval processes and approaches toward genome editing and gene drive, the discussion section explores the implications and broader significance of these findings. By synthesizing the results of the literature search and survey analyses, this section aims to elucidate key insights, identify challenges, and propose avenues for future research and policy development concerning genetic engineering applications and biotechnology regulation across African countries.

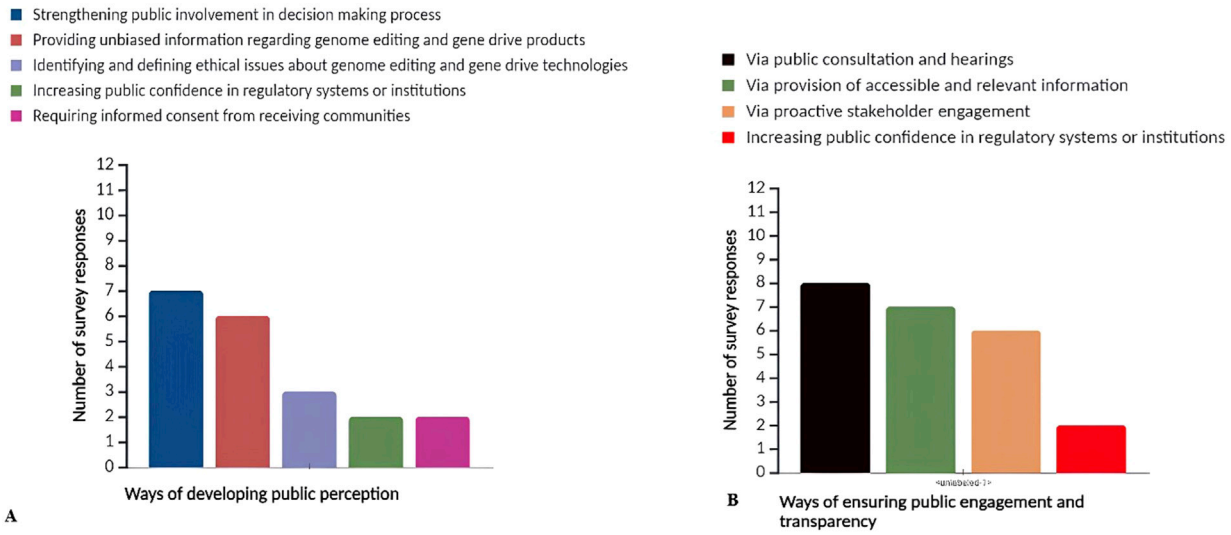

FIGURE 3
The survey response analysis on: **(A)** ways of public perception and attitude development towards genome editing and gene drive technologies/products; **(B)** ways to ensure public engagement and transparency in the decision-making process towards genome editing and gene drive technologies and products.

TABLE 4 The survey results on some African countries plan to draft or modify their existing regulations for genome editing and gene drive technologies.

Countries	Plans to modify the regulatory framework under their purview?	How modification will be made	Willingness to learn practices and experiences from others?	Readiness to share practices and experiences?
Benin	–	Through the development of specific guidelines and regulatory policies for these technologies	+	+
Ethiopia	+	Through the development of specific guidelines and regulatory policies for these technologies	+	+
Democratic Republic of Congo	+	Through the development of specific guidelines and regulatory policies for these technologies	–	–
Gambia	+	Need revision. Global Environment Facility allocated funds for an update	+	+
Mozambique	+	Through the development of specific guidelines and regulatory policies for these technologies	+	+
Tunisia	+	Through the development of specific guidelines and regulatory policies for these technologies	+	–
Uganda	+	Through the development of specific guidelines and regulatory policies for these technologies	+	+
Zambia	+	By modifying the biosafety regulations	+	+

(Mark +: denotes yes; -: denotes "No").

4.1 Authorization of genetic engineering applications in Africa

The regulatory framework landscape for genetic engineering applications in Africa varies significantly between countries. While some countries have enacted comprehensive regulations for the use of GMOs, others have more outdated regulatory frameworks. Several African countries have biosafety regulatory frameworks that can approve genetic engineering applications in CFTs, open field trials, commercialization and importation for use as food or

TABLE 5 Status on authorization for genetic engineering applications in African countries according to scientific literature.

Country	Stages of development					References
	Laboratory research	CFTs	Open-field cultivations	Pre-market authorization	Importing for direct use	
Angola	+	–	–	–	–	• Muzhinji and Ntuli, (2020) • Angola succeeds in the Application of Biotechnology in Agriculture (Digital, 2022)
Benin	–	–	–	–	–	• GM crops are officially banned in Benin • There is a legal vacuum reflected by the lack of an organizational framework for regulating the production, commercialization, and importation of GM crops (Houdegbe et al., 2018)
Burkina Faso	+	+	+	+	+	• A "non-gene drive male-biased" application was authorized in July 2021 by the ANB (National Biosafety Agency) for import (Pablo, 2023) • However, no more genetically modified mosquitoes released in 2021 (Pablo, 2023) • The first phase took place in July 2019 with the release of 6,400 transgenic mosquitoes in Bana (a rural village in the center west of the country) (Vekcha, 2022) • Cowpea with GM insect resistance undergoing confined field trial (Akinbo et al., 2021) • Commercial release of Bt-cotton but put on hold in 2016 due to decision to terminate the commercial registration of GM cotton • CFTs of several GM crops — cassava, cowpea, banana, and Irish potato - are taking place (Wadvalla, 2022)
Botswana	–	–	–	–	–	Muzhinji and Ntuli (2020)
Comoros	+	–	–	–	–	Muzhinji and Ntuli (2020)
DRC	+	–	–	–	–	• Lack of adequate legislation to regulate and approve the import and to monitor the introduction of GMOs and synthetic biology products (Otono et al., 2020)
Eswatini	+	+	+	+	+	• Approved GM crop application (Wadvalla, 2022) • The commercial release of transgenic insect resistant Cotton has been approved (Akinbo et al., 2021)
Ethiopia	+	+	+	+	–	• Developing transgenic Enset resistant to bacterial wilt (Conrow, 2018) • Development of lodging resistance in tef (*Eragrostis tef*) (Beyene et al., 2022) • Insect-resistant and drought tolerant Maize under confined field trials (Akinbo et al., 2021) • TELA Maize, (drought tolerance plus insect resistance (Conrow, 2018; ABNE, 2022) • Open cultivation for Bt cotton (ABNE, 2022) • Approved commercial cultivation for insect-resistant, Bt cotton hybrids (Conrow, 2018; Gebretsadik and Kiflu, 2018; Terefe, 2018; Komen et al., 2020)
Gambia	–	–	–	–	–	–
Ghana	+	+	+	–	–	• Nitrogen and water-use-efficient (NEWEST) rice and genetically modified cowpea (Baffour-Awuah, 2022) • CFTs of several GM crops — cassava, cowpea, banana and Irish potato are taking place in Ghana (Wadvalla, 2022) • These two transgenic crops have gone through various stages of evaluation and field trials (Baffour-Awuah, 2022)

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10.3389/fbioe.2024.1483279

TABLE 5 (*Continued*) Status on authorization for genetic engineering applications in African countries according to scientific literature.

Country	Stages of development					References
	Laboratory research	CFTs	Open-field cultivations	Pre-market authorization	Importing for direct use	
						• An application for commercial release has been requested and invited public comments to make a final decision on the request (Baffour-Awuah, 2022)
Kenya	+	+	+	+	+	• The National Biosafety Authority (NBA) has reviewed over 28 contained use applications (Njiraini, 2020) • NBA has approved confined field trials (Njiraini, 2020) • CFTs of several GM crops — cassava, cowpea, banana, and Irish potato - are taking place (Wadvalla, 2022) • NBA has reviewed two environmental release applications for Bt cotton and Bt maize (Njiraini, 2020) • Drought-tolerant maize approved for National performance trials (NPTs) (Komen et al., 2020) • NBA approved GM cassava resistant to brown streak virus disease (CBSD) for environmental release (Maina, 2022c) • The importation of White transgenic Maize (Maina, 2022a)
Madagascar	–	–	–	–	–	• No research and development, and no confined field trial (Muzhinji and Ntuli, 2020)
Malawi	–	+	–	+	–	• Bt cowpea and virus-resistant bananas are undergoing confined field trials (Malawi Progresses in GM Crop Trials - Chaweza (2020)) • Commercial release of transgenic insect resistance of Cotton approved
Mauritius	+	–	–	–	–	• Transgenic Sugarcane research is ongoing (Muzhinji and Ntuli, 2020)
Mozambique	+	+	–	–	–	• Conducting confined field trials for drought tolerant maize (Muzhinji and Ntuli, 2020) • CFTs of several GM crops — cassava, cowpea, banana, and Irish potato - are taking place (Wadvalla, 2022)
Namibia	–	–	–	–	–	• No transgenic crops are approved for environmental release (Muzhinji and Ntuli, 2020)
Nigeria	+	+		+	+	• Several transgenic crop research undergoing • Several transgenic crops, such as Cassava, Sorghum and Maize, are undergoing CFTs research • CFTs are completed for TELA maize (Maina, 2022) • National varieties release committee plans to evaluate TELA maize for approval before it is made commercially available for the 2023 season (Maina, 2022) • General release and submission for variety registration for insect-resistant cowpeas (Komen et al., 2020; ABNE, 2022) • TELA is first transgenic maize variety to move toward adoption (Maina, 2022)
South Africa	–	–	–	+	+	• Farmers are commercially growing TELA maize (drought- and insect-tolerant) (Maina, 2022) • Herbicide-tolerant soybean commercially released (Muzhinji and Ntuli, 2020) • Importation of transgenic Bt white maize and TELA maize authorized (Maina, 2022)

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TABLE 5 (*Continued*) Status on authorization for genetic engineering applications in African countries according to scientific literature.

Country	Stages of development					References
	Laboratory research	CFTs	Open-field cultivations	Pre-market authorization	Importing for direct use	
Tanzania	+	+	–	–	–	• Transgenic virus-resistant cassava under development • Researchers conducting CFTs for drought-resistant maize and virus-resistant cassava (Muzhinji and Ntuli, 2020)
Tunisia	+	–	–	–	–	• Does not import any GM food or feed (banned) (FAO, 2019)
Uganda	+	+	+	+	–	• Weevil-resistance sweet potato and herbicide-tolerant soybean are under lab research (Ghislain et al., 2018; ABNE, 2022) • Has approved field experiments involving transgenic crops (Zawedde et al., 2018) • RNAi-mediated resistance to Cassava brown streak disease (CBSD) (Odipio et al., 2013; ABNE, 2022) • CFTs of several GM crops — cassava, cowpea, banana, and Irish potato - are taking place (Wadvalla, 2022) • Several transgenic crops are undergoing multiplication trials (Zawedde et al., 2018) • For some transgenic crops, multi-location trials are completed and awaiting biosafety decision regarding environmental release (Zawedde et al., 2018)
Zambia	+	–	–	–	–	• Lab research is authorized but no CFTs, open field trials, and environmental release authorization for transgenic crops (Muzhinji and Ntuli, 2020)

(Mark "+": denotes the availability of scientific evidence for the approval of genetic engineering application at various stages; "-": denotes "no scientific evidence available for approval of genetic engineering application at various stages).

10.3389/fbioe.2024.1483279

TABLE 6 The literature findings analyzed from academic journals on the status of genome editing and gene drive technologies in African countries.

Country	Gene Editing				
	Laboratory Development and Biosafety regulatory framework development status[a]	Contained trial[b]	Confined trials/Small-scale field release[c]	Open-scale field release[d]	Multiplication field trials/Large-scale controlled field releases[e]
Burkina Faso	• Started considering developing genome-editing policies (Tripathi et al., 2022) • Community and stakeholder engagement work done (Toe et al., 2022)	–	–	–	–
Eswatini	• Lab facilities are organized • Started considering developing genome-editing policies (Tripathi et al., 2022)	–	–	–	–
Ethiopia	• Started considering developing a genome-editing regulatory framework (Tripathi et al., 2022)	• Lodging resistance in Teff successfully developed using CRISPR/Cas9-based genome editing (Beyene et al., 2022) • CRISPR-Cas9 has potential to be used for Enset to combat wilting (Merga et al., 2019)	–	–	-–
Ghana	• Lab facilities are organized and started considering developing genome-editing policies (Tripathi et al., 2022)	–	–	–	–
Kenya	• NBA published guidelines suitable for regulating genome-edited organisms and products (ISAAA, 2022) • CRISPR/Cas9-based research in yam (Dioscorea spp.) to induce site-specific disruption of PDS gene developed (Syombua et al., 2021)	+	+	+	• Researchers applied for approval of multiplication trials • Six applications approved for contained use
Malawi	• Genome Editing Guidelines approved, joining Nigeria and Kenya. (ISAAA, 2022)	–	–	–	–
Nigeria	• Nigeria has become first African country to publish national biosafety guidelines for genome editing regulation (USDA, 2021; Tripathi et al., 2022)	• Guidelines are issued for gene editing of plants, animals, and microorganisms, covering containment, field trials, commercial/general release and imports for food or feed (Tripathi et al., 2022)	+	+	• Approval for multiplication trials for genome editing products on a case-by-case basis (Tripathi et al., 2022)
South African	• Currently developing regulatory policies for genome editing (Tripathi et al., 2022)	–	–	–	–
Sudan	• Lab facilities are developed • Started considering developing genome-editing policies (Tripathi et al., 2022)	–	–	–	–
Uganda	• Drafting guidelines for gene-edited crops through NBC support • Contained facility laboratory to be established for contained trials of male sterile mosquitoes • No field trials with gene-edited crops yet (Ongu et al., 2023)	–	–	–	–

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TABLE 6 (*Continued*) The literature findings analyzed from academic journals on the status of genome editing and gene drive technologies in African countries.

Country	Gene Editing				
	Laboratory Development and Biosafety regulatory framework development status[a]	Contained trial[b]	Confined trials/Small-scale field release[c]	Open-scale field release[d]	Multiplication field trials/Large-scale controlled field releases[e]
Zimbabwe	• Lab facilities are organized and started developing genome-editing policies (Tripathi et al., 2022)	–	–	–	–
Country	**Gene Drive**				
	Laboratory research	Contained trial	Confined trials/Small-scale studies	Open-scale field release	
Burkina Faso	• Researchers anticipate the release of genetically engineered mosquitoes to initiate gene drives aimed at reducing insect populations (Swetlitz and Stat, 2024) • Existing guidelines for non-gene drive mosquitoes can provide an overall framework for gene drive technology on case-by-case basis (Toe et al., 2022)	–	–	• Target Malaria plans to conduct the first field trials of gene drive mosquitoes in partner countries like Uganda, Burkina Faso or Ghana within 5–10 years (Scudellari, 2019)	
Ethiopia	• No research at the laboratory level • African Union declared commitment to invest in the development and regulation of gene-drive technology (AUDA-NEPAD, 2023)	–	–	–	
Kenya	• No gene drive research at the laboratory level yet	–	–	–	
Nigeria	• In August 2019, the "National Biosafety Management Agency (NBMA) Act 2015" accepted emerging agricultural biotechnologies - gene drive, gene editing, and synthetic biology (NBMA, 2015) • A journalist was trained on the controversies surrounding "gene drives" research, aiming to equip journalists with the necessary understanding of the issues surrounding gene drive (Omoniyi, 2024)	• A person or institution shall not carry out gene drive, gene editing, and synthetic biology except with the approval of the Agency (NBMA, 2015)	–	–	
Uganda	• The GMO Bill, with little mention of gene drive, has been one of the most debated bills in Uganda's history (Bendana, 2020) • The President refused to approve the 2018 GMO Bill due to ecological and health concerns (Duba, 2021)	–	–	• No gene drive organism has yet been tested in the field (Yao et al., 2022) • Uganda may host the first field trials of gene drive mosquitoes for malaria control (Scudellari, 2019; Hartley et al., 2024) • Decision on whether to release gene drive mosquitoes is yet to be made (De Graeff et al., 2021)	

(Mark "+": denotes availability of scientific evidence indicating approval for genome editing and gene drive application at various stages; "-": denotes no scientific evidence available for approval for genome editing and gene drive application at various stages.

[a]Indicates the progress in laboratory research and the status of biosafety regulatory frameworks that guide the development of genome editing and gene drive technologies.

[b]Refers to trials conducted in highly controlled environments, such as greenhouses or laboratories, where genome-edited organisms are kept isolated to prevent unintended environmental exposure or risks.

[c]Highlights small-scale field trials conducted under regulated conditions, where genome-edited organisms are tested outdoors in confined areas.

[d]Represents large-scale, less confined field trials where genome-edited organisms are released into the environment under supervision.

[e]Shows the status of large-scale controlled field releases, where genome-edited organisms are grown in significant quantities.

feed, while many African countries have no experience in authorizing CFTs or even have a biosafety regulatory framework at all (ABNE, 2023).

The survey findings (Table 1) and literature review (Table 5) reveal both consistent patterns and new insights. In several countries, such as Eswatini, the Democratic Republic of Congo (DRC), Kenya, Mozambique, and Nigeria, the approval processes for genetic engineering applications appear to be interrelated and mutually supportive. However, the survey also introduces new information not previously documented in the literature. For instance, Ethiopia and Ghana have authorized the full spectrum of genetic engineering applications, including the importation of GM plants for direct use. Additionally, Zambia has approved genetic engineering for R&D, CFTs, and the importation of GM crops for food and feed—details that have not been reported in earlier studies. In cases where survey data were unavailable, such as Burkina Faso, Malawi, and Mauritius, the literature review helped fill gaps and validate the survey results.

Eleven countries (Burkina Faso, Egypt, Eswatini, Ethiopia, Ghana, Kenya, Malawi, Nigeria, South Africa, Sudan, and Zambia) have approved GM crop applications, although Zambia has yet to establish biosafety laws regulating GMOs (ABNE, 2022; ISAAA, 2024 as reviewed in Mmbando, 2024). The other ten countries have conducted field trials and approved the commercial cultivation of GM crops (Mmbando, 2024). Despite several field trials and commercial release authorizations, African countries continue to bear the reputation of being slow adaptors of GM technologies, mainly attributed to overly restrictive biosafety regulatory frameworks (Ongu et al., 2023) and political challenges (Komen et al., 2020) often exacerbated by anti-GMO activism which slowed or halted the adoption of biosafety legislation (Entine, 2022). These challenges hinder the testing and adoption of new crop varieties, including those developed by genome editing or other advanced technologies, which aim to enhance income and reduce the environmental impact of agriculture (Komen et al., 2020). Notably, African researchers are working tirelessly to develop biotechnology products so that Africa is no longer a battleground for adopting GMOs (Muthie, 2022).

According to data retrieved from ABNE in August 2023, countries such as Ghana, Tanzania, Mozambique, and Uganda have experience approving CFTs. Additionally, Burkina Faso, Nigeria, Sudan, Ethiopia, Kenya, Malawi, and Eswatini have approved commercial cultivation of GM crops. In particular, Eswatini, Ghana, Kenya and Nigeria are the front liners in the development and maturation of national biosafety laws and, hence, they have authorized the genetic engineering applications for several activities (Table 1). In contrast, Benin has not approved any commercial release or importation of GMOs. Despite the existence of relevant institutions in Benin, a legal vacuum appears to persist, reflected in the absence of an organizational framework for regulating the production, commercialization and importation of GMOs (IOBC-WPRS, 2023).

CTFs have been approved for various crops in several African countries: maize, cotton, sorghum, cassava and sweet potato in Kenya; cassava, cotton, cowpea, rice and soybean in Nigeria; banana, cassava, maize, potato and rice in Uganda, and; cotton, cowpea, banana and plantains in Malawi (Komen et al., 2020) (Table 5). Additionally, CFTs for GM crops — such as cassava, cowpea, banana and Irish potato are taking place in Mozambique, Kenya, Uganda, Ghana, Burkina Faso and Rwanda (Wadvalla, 2022). In contrast, Zambia, Tunisia and the DRC have not yet authorized CFTs, according to ABNE. This lack of authorization could be due to the lack of appropriate legislation to regulate the importation of GMOs and to monitor their introduction (Otono et al., 2020) (Table 5). The DRC is currently considering revising or strengthening its biosafety framework (Otono et al., 2020).

Ghana stands out as a West African country that have approved genetic engineering applications for laboratory research, CFTs, open-field trials and commercial cultivation. In 2012, the National Biosafety Committee in Ghana approved multi-locational trials for insect-resistant GM cotton after accepting data from CFTs conducted previously in Burkina Faso (Komen et al., 2020). Genetically modified nitrogen- and water-efficient rice and pod borer-resistant cowpeas have not been commercialized yet, although they have undergone various stages of evaluation and field trials (Baffour-Awuah, 2022).

In general, most African countries have not yet fully overcome the challenges associated with GMOs. These hurdles may pose difficulties in adapting to new regulatory frameworks and governance of emerging technologies such as genome editing and gene drive (Masehela and Barros, 2023).

4.2 Status of genome editing and gene drive regulatory frameworks in Africa

Genome editing technology is increasingly attracting the interest of African researchers due to its potential to address agricultural, health and environmental issues. To fully benefit from genome editing, there are calls that products developed through this technology must be subjected to reasonable, science-based regulation (Entine et al., 2021). Globally, while some countries have quickly adapted or amended their legislation to support the use of genome editing, others are in the initial stages of policy development (Jenkins et al., 2021). However, some countries still categorize all organisms derived through genome editing as GMOs (Hundleby and Harwood, 2022).

In Africa, the regulatory landscape is varied. Some countries have enacted regulatory frameworks despite not yet utilizing crop genetic engineering technology, while others have already conducted field trials and are beginning to authorize GM crops for cultivation (Komen et al., 2020; ABNE, 2022). This study found that few African countries have developed specific regulatory approaches tailored to genome-editing. For instance, the survey analysis (Table 2) highlights that countries like Benin, Eswatini, Kenya, Nigeria, and Uganda have established governance frameworks for genome editing, an observation also supported in the literature (Meeme, 2021; Genetic Literacy Project, 2021; Wadvalla, 2022; Buchholzer and Frommer, 2023). Additionally, Burkina Faso and Ghana have begun considering developing policies for genome editing (Tripathi et al., 2022) (Table 6).

Nigeria was the first African country to publish its regulatory frameworks on genome editing in December 2020, followed by Kenya, which published its frameworks in February 2022, an important milestone regulatory development for genome editing in Africa (ISAAA, 2022). Rather than amending its biosafety act,

Kenya's National Biosafety Authority (NBA) opted to develop a guideline on genome editing (Komen et al., 2020).

Malawi also approved its regulatory frameworks for genome editing in August 2022 (ISAAA, 2022), and Burkina Faso has validated the national regulatory frameworks, which are awaiting final approval and publication (AUDA-NEPAD, 2023). Burkina Faso is, therefore, expected to become the fourth African country to approve and publish national biosafety regulatory frameworks for genome editing. Eswatini, too, has made significant progress in establishing regulations for genome editing (Meeme, 2021).

Although Benin, Eswatini and Uganda have not yet formally published their regulatory frameworks for genome editing and gene drive, their existing biosafety regulations could be applied to oversee these technologies. This approach is similar to the EU regulatory framework, where existing biosafety regulations are applied without amendments, requiring prior government safety approval, which is the most stringent regulation for genome editing products (Tachikawa and Matsuo, 2023). Furthermore, the survey findings show that the regulatory frameworks in Benin, Eswatini, and Uganda include provisions for genome editing and gene drive technologies, deregulating SDN-1 and SDN-2 techniques while regulating SDN-3 on a case-by-case basis (Table 2). However, a detailed investigation into the regulatory status of genome editing and gene drive technologies in these African countries remains largely unexplored in the scientific literature. On the other hand, in Burkina Faso, Ethiopia, Ghana, South Africa, Sudan, and Zimbabwe, lab facilities have been developed and initiated developing genome editing policies (Tripathi et al., 2022) (Table 6). Moreover, survey results from Burkina Faso, Cameroon, Kenya, Liberia, Mali, Nigeria, South Africa, and Uganda claimed that there are ongoing research activities on Gene Drive Modified Mosquito (GDMM) in the laboratory phase and emphasized the importance of a regulatory framework (Finda et al., 2023). Several African countries, including the DRC, Ethiopia, Gambia, Ghana, Mozambique, Tanzania, Tunisia, and Zambia, lack biosafety regulatory frameworks governing genome editing and gene drive technologies. However, Ethiopia, Ghana, Sudan, South Africa and Zimbabwe have begun considering the development of such frameworks (Jenkins et al., 2021; Tripathi et al., 2022; Africa, 2022). The absence of clear regulatory frameworks in these countries poses a challenge to the development, adoption and implementation of genome editing and gene drive technologies. In response, several African countries have shown interest in revising or adapting their existing regulatory frameworks to accommodate these emerging biotechnologies (Meeme, 2021).

The survey found that biosafety experts and regulators in the DRC, Gambia, Ghana, Mozambique, Zambia and Tanzania are interested in amending their biosafety regulatory frameworks to regulate genome editing and gene drive products effectively. By doing so, these countries aim to fully leverage the potential of genome editing and gene drive technologies.

4.3 Challenges in implementing and harmonizing biosafety regulatory frameworks in Africa

African countries face significant challenges in developing and implementing regulations for genome editing and gene drive technologies. Addressing these gaps is crucial for ensuring the responsible and ethical use of these technologies. Our survey analysis identified several key challenges, including a lack of public trust, opposition, and moral concerns regarding genome editing and gene drive technologies. Public trust is critical to the successful adoption and realization of the benefits of these technologies on the African continent (Masehela and Barros, 2023).

The survey revealed that limited resources, a lack of trained and skilled expertise, insufficient public awareness, and public resistance or scepticism had hindered the implementation of national biosafety regulations for genome editing and gene drive technologies. Masehela and Barros (2023) also noted that the lack of trained technical expertise, inadequate intellectual property rights infrastructure and various concerns on genome editing products and unsupportive government leadership remain prevalent on the African continent. Similarly, Maruta et al. (2023) highlighted that insufficient infrastructure, training, capacity building and financing affect efforts to strengthen biosafety in African nations. Enhancing expertise for the development of regulatory frameworks for genome editing or gene drive technology could increase the legitimacy of the overall assessment process (Adenle et al., 2013).

Our survey analysis further indicates that negative public perception is a significant barrier, primarily due to the perceived lack of relevant data about the technologies as they are still in their early stages of development, together with fears about their potential unintended consequences or misuse. Abkallo et al. (2024) reported that mistrust surrounding genome editing technology arises from ethical concerns, fears of unintended consequences and a lack of transparency in communication, which hinder its widespread acceptance and implementation in African nations. Public perception can significantly impact gene editing technology implementation; thus, both public and stakeholder acceptance is crucial for favorable regulations and deployment (Strobbe et al., 2023).

Unharmonized regulations, especially with respect to definitions and risk assessment approaches, can hinder the applications of these technologies and future trade between countries. Therefore, harmonizing the regulatory climate is essential for equitable access and international trade in technology products (Hundleby and Harwood, 2022). However, several challenges impede the harmonization of the biosafety regulatory framework in African countries. Our survey found that the lack of coordination and information-sharing among regulatory agencies, issues related to technology transfer, concerns about intellectual property rights, the absence of region-specific regulatory frameworks for genome editing, the existence of different regulatory frameworks and definitions, and difficulties in aligning different cultural, social, and ethical perspectives were cited as major obstacles to harmonizing biosafety regulatory frameworks at the regional level. This finding is supported by a report (Africa, 2016) highlighting that significantly different legislation, definitions, and regulatory approaches among countries hinder regional or international harmonization. The report emphasized the importance of cooperation and harmonization among regulators to prevent arbitrary decisions, regional and international asymmetries in scientific and technical development, and trade barriers.

To address these challenges, it is crucial for African countries to collaborate, discuss, debate and attempt to harmonize their science-

based regulatory frameworks. According to the chief executive of Kenya's National Biosafety Authority (NBA), many countries in the Global North have adopted a common approach to regulating these new technologies, so there is an opportunity for the Global South to learn from them in developing approaches for these new technologies, by promoting greater international collaboration in knowledge sharing and figuring out how to best utilize new technologies that are being developed or used in their own countries (Ladenheim, 2023). This will prepare them for the eventual approval and use of products developed using genome editing approaches (Masehela and Barros, 2023). Regulatory diplomacy can play a critical role by facilitating dialogue and collaboration, ensuring that diverse perspectives are captured in cohesive regulatory approaches (Warner and Pink, 2024). Such collaborative efforts can foster a more cohesive regulatory environment, facilitating the responsible development and deployment of genome editing technologies across the continent.

4.4 Challenge-driven opportunities for developing biosafety regulatory framework in Africa

Africa faces an urgent need to close the yield gap in staple crops and increase food production to feed the growing population (Tripathi et al., 2022). The challenge of producing more food with the same or less land and water, improving nutrition and helping farmers adapt to climate change is particularly acute (Searchinger et al., 2024). Climate change is predicted to negatively impact the African food system, as agriculture in the region is largely dependent on rain-fed farming and subsistence agriculture (Manners et al., 2021). Additionally, climate change may drive the expansion of disease vectors and vector-borne pathogens like dengue, Zika, and Chikungunya viruses (De Souza and Weaver, 2024), creating suitable temperature conditions for transmission beyond current limits (Samy et al., 2016; Minigan et al., 2018; Kraemer et al., 2019; Ryan et al., 2019). These challenges underscore the need to scale up research, build capacity, and develop genome editing and gene drive technologies within appropriate regulatory frameworks. Realizing the full potential of new breeding tools, such as genome editing, alongside conventional technologies is essential (Pixley et al., 2019).

To leverage these advancements, African countries must develop new regulatory frameworks or adjust existing biosafety regulatory frameworks to accommodate genome editing and gene drive technologies, perhaps drawing on models of Nigeria (USDA, 2021) and Kenya (ISAAA, 2022). In this context, adopting adaptive regulatory frameworks will enable African countries to respond more effectively to the rapid developments in genome editing and gene drive technologies while addressing public concerns and ethical considerations (Greer and Trump, 2019).

In regions with low awareness and high public resistance to genome editing and gene drive technologies, effective regulation can assure society that these technologies will not be misused. Building public trust is critical to the success and acceptance of these technologies (Masehela and Barros, 2023) while addressing concerns related to safety (Trump et al., 2023).

The regulatory challenges encountered with GM crops provide valuable lessons that can inform the development of regulatory frameworks for genome editing and gene drive technologies (Rock et al., 2023). These experiences offer an opportunity to create more robust and informed regulatory frameworks.

4.5 Strengthening the regulatory landscape in Africa

Our survey analysis highlights the importance of investing in training programmes and workshops for regulators and stakeholders to strengthen the regulatory framework for genome editing and gene drive technologies. Establishing partnerships with academic institutions for research and capacity building, along with increasing knowledge-sharing with international organizations and experts, emerged as key strategies to enhance the regulatory framework in African nations.

Enhancing research and development capacities through international collaboration has already shown promising results. For instance, Nigeria, Kenya and Uganda have significantly advanced their plant genome editing technology capacities through partnerships with the International Institute of Tropical Agriculture (IITA) and the Swedish University of Agricultural Sciences (SLU) (Ongu et al., 2023). Such collaborations provide a blueprint for other African countries to strengthen their regulatory landscape.

A critical element in this process is the proactive engagement of diverse stakeholders, including policymakers, scientists, the public and educators, in open and accessible dialogues concerning the scientific principles, potential benefits and risks associated with genome editing (Abkallo et al., 2024) may ensure a more inclusive and transparent regulatory process. Public participation, transparency and accountability are crucial elements in policy development and agenda-setting, playing a significant role throughout the regulatory pathway (Nielsen et al., 2021). Without the bottom-up regulatory structures involving public engagement and the pursuit of people-centered, measures to hold researchers accountable for unethical research practices could be weak (Barbosa et al., 2021). Incorporating this approach can help address public concerns, build trust and ensure that the regulatory frameworks are comprehensive and well-informed by a wide range of perspectives and expertise.

5 Conclusion

The regulatory landscape for genome editing and gene drive technologies in Africa is diverse and evolving. Our study has highlighted significant disparities in the development and implementation of biosafety frameworks across different countries. While nations such as Nigeria and Kenya have made notable strides in establishing regulatory frameworks specific to genome editing, others are still in the preliminary stages of policy formulation. The findings indicate that the lack of clear, harmonized regulations poses challenges to the adoption and application of these technologies. Additionally, issues such as limited resources,

inadequate technical expertise and public scepticism further complicate the regulatory environment.

Despite these challenges, there is a strong interest among African countries to harness the potential of genome editing and gene drive technologies to address pressing agricultural, health and environmental issues. The successful implementation of these technologies will require comprehensive regulatory frameworks that are science-based, context-specific and adaptable to emerging innovations. It is also evident that building public trust through transparent communication and stakeholder engagement is crucial for the acceptance and success of these technologies.

6 Actionable recommendations

Based on the findings of this study, the following recommendations are proposed to strengthen the regulatory frameworks for genome editing and gene drive technologies in Africa:

1. Build Capacity and Provide Training: Continue offering comprehensive training programmes and workshops for regulators and stakeholders. While traditional programmes remain important, also explore innovative approaches such as inter-agency consultations and internships in countries with established practices. These initiatives will equip local regulators and technical advisors with the practical experience and knowledge needed to contribute to informed decision-making and effective regulatory oversight.
2. Foster International Collaboration: Promote partnerships with international organizations, academic institutions and experts to facilitate knowledge transfer and technical assistance. By fostering international cooperation, countries can benefit from shared expertise in developing robust regulatory frameworks. Emphasize regulatory diplomacy to navigate global advancements, ensuring Africa's regulatory systems remain aligned with global developments.
3. Adopt Best Practices: Incorporate best practices from countries with established regulatory frameworks, such as Nigeria and Kenya. While leveraging these successful models, tailoring them to the unique contexts and needs of other African nations is crucial. This ensures that the regulatory process becomes more relevant and adaptable to each country's specific challenges and opportunities.
4. Develop Context-Specific Regulatory Frameworks: Formulate flexible regulatory frameworks that can accommodate ongoing technological advancements. These frameworks should address local ethical, social, and environmental considerations. This approach can help empower African countries to develop regulations that reflect their national aspirations together with their specific context and challenges.
5. Harmonize Approaches that Underpin Regulatory Decision-Making: Align key regulatory decision-making components, such as definitions and risk assessment methodologies, across African countries. This alignment can reduce inconsistencies and asymmetries between national regulatory systems while preserving flexibility for local adaptations. Additionally, recognize technical data, analyses, and assessments from foreign or neighboring regulatory authorities, reducing duplicative work and increasing the efficiency of regulatory authorizations. This will help lower costs and create smoother, faster approval processes.
6. Encourage Stakeholder Involvement: Engage a broad range of stakeholders, including scientists, policymakers, industry representatives and the public (including indigenous people and local communities). Ensuring their active participation in the regulatory process can lead to more comprehensive, widely accepted regulatory frameworks. Inclusive consultations help bring diverse perspectives to the table, improving the quality and transparency of regulations.
7. Engage the Public and Educate: Implement innovative education campaigns to raise public awareness about the potential benefits and risks of genome editing and gene drive technologies. Transparent and accessible communication can mitigate public skepticism, foster trust in the regulatory process, and support informed decision-making. Ensuring that the public understands the science and the risk management in place would lead to greater acceptance of these technologies.

By implementing these recommendations, African countries can develop robust and adaptive regulatory frameworks that support the safe, ethical and beneficial use of genome editing and gene drive technologies. This proactive approach will help enable the continent to address critical challenges in agriculture, health and environmental sustainability, ultimately contributing to improved livelihoods and economic development.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

This study involved the collection of data through surveys and did not require formal ethical review or approval in accordance with relevant legislation and institutional guidelines. Participation in the survey was voluntary, and participants provided their informed consent by completing the survey. No personally identifiable information was collected, and all responses were anonymized to ensure privacy and confidentiality in line with relevant regulations and institutional requirements.

Author contributions

TR: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing–original draft. FM-B: Conceptualization, Formal Analysis, Investigation, Methodology, Writing–review and editing, Data curation. WC: Conceptualization, Methodology, Resources, Supervision, Writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY
Clara Rubinstein,
Institute for Scientific Cooperation in Environment and Health (ICCAS), Argentina

REVIEWED BY
Jan-Hendrik Groenewald,
Biosafety South Africa, South Africa
Drew Lloyd Kershen,
University of Oklahoma, United States

*CORRESPONDENCE
Olalekan Akinbo,
akinbooa@gmail.com

†These authors have contributed equally to this work

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Africa and zero hunger agenda: genome editing policy landscape, challenges and opportunities

Olalekan Akinbo[1*†], Bongani Nkhabindze[1], Josephine Amedu[2], Rufus Ebegba[2], Agnes Asagbra[2], Billy Omboki Ratemo[1], Susan Angira Dada[1], Anne Muia[3], Roy Mugiira[3], Lilian Chimphepo[4], Leeford Oko Wristberg[5], Mathurin W. Rouamba[6], Koussao Some[6], Valter N. A. Nuaila[7], Alsácia Atanásio[7], Olufunke Bolatito Shittu[8], Charles Oluwaseun Adetunji[9], Loubna Hamidi[10], Elinasi Monga[10], Silas Obukosia[1], Muyiwa Seyi Adegbaju[11†], Samuel Acheampong[12] and Estherine Fotabong[1]

[1]African Union Development Agency – NEPAD (AUDA-NEPAD), Directorate of Agriculture, Food Security and Environmental Sustainability, Midrand, South Africa, [2]National Biosafety Management Agency, Abuja, Nigeria, [3]National Biosafety Authority, Nairobi, Kenya, [4]National Biosafety Authority, Lilongwe, Malawi, [5]National Biosafety Authority, Accra, Ghana, [6]Agence Nationale de Biosécurité (ANB), Ouagadougou, Burkina Faso, [7]Centro Nacional de Biotecnologia e Biociencias (CNBB), Maputo, Mozambique, [8]Department of Microbiology, College of Bioscience, Federal University of Agriculture, Abeokuta, Nigeria, [9]Department of Microbiology, Edo State University, Auchi, Nigeria, [10]International Union for Conservation of Nature (IUCN), Dar es Salaam, Tanzania, [11]Department of Biomedical Sciences, College of Health Sciences and Technology, Rochester Institute of Technology, Rochester, NY, United States, [12]Department of Molecular Biology and Biotechnology, University of Cape Coast, Cape Coast, Ghana

Africa has historically struggled to adopt innovative agricultural technologies, which has significantly hindered efforts to ensure food security and improve livelihoods over the past century. A major obstacle in this regard has been the persistent skepticism surrounding the potential benefits of agricultural biotechnology. The challenges contributing to this skepticism include a notable knowledge gap among stakeholders, widespread technophobia, or fear of technology, as well as inconsistencies with global agreements such as the Convention on Biological Diversity (CBB). Although these challenges are not exclusive to Africa, they disproportionately impact the continent, making the need for effective solutions even more urgent. This paper investigates the national government policy landscape in five African countries that are poised to create a regulatory environment conducive to deploying genome editing technology for improved agricultural productivity. This exploration aligns with the continental agricultural policy initiatives, notably the "CAADP Malabo Declaration" and the soon-to-be-signed "CAADP Kampala Declaration." Aligning with the African Union's continental agenda on agricultural transformation, as outlined in the Malabo Declaration and other key documents, is crucial for adopting innovative agricultural technologies like genome editing. Such alignment becomes increasingly critical for realizing the objectives set forth in the post-Malabo Declaration, with the Kampala Declaration playing a vital role in its implementation. This cohesive approach

will not only foster agricultural innovation but also expedite development across the continent, addressing the pressing needs of food security and livelihoods in Africa.

KEYWORDS

food security, genome editing, technophobia, policy landscape, agriculture biotechnology

1 Introduction

Global society and governments face the significant challenge of feeding over 7 billion people. In response, the United Nations established Agenda 2030 on Sustainable Development Goals (SDGs) to achieve peace and prosperity worldwide. Among the goals, Sustainable Development Goal 2 aims for zero hunger by ensuring food security and nutrition through sustainable agriculture. The magnitude of this issue is underscored by alarming statistics: in 2019, approximately 8.9% (690 million) of the global population suffered from hunger, while about 2 billion people were deprived of safe, nutritious, and adequate food. Notably, over 50% of these individuals reside in Asia, with 205 million in Latin America and a striking 675 million in Africa.

The Food and Agriculture Organization (FAO) defines "hunger" as "an uncomfortable or painful physical sensation caused by insufficient consumption of dietary energy." This sensation becomes chronic when an individual consistently fails to consume enough calories to maintain a normal, active, and healthy life. Hunger is particularly prevalent on the African continent, where the prevalence of undernourishment (POU) was about 192.6 million in 2005—this number increased to 250 million by 2019. Projections suggest that the POU could reach 433 million by 2030.

Climate change significantly exacerbates food insecurity globally, impacting approximately 700 million people who face food insecurity due to climate-related factors, as noted by IFAD and WHO. (2020). Rising temperatures associated with climate change reduce water availability for agricultural use, while land scarcity driven by urbanization, population growth, and desertification further constrains agricultural production. Specifically, the effects of increasing temperatures intensify water scarcity by increasing evaporation from water sources, altering precipitation patterns, and accelerating the melting of glaciers and snowpack, all of which disrupt the reliability of water supplies for agricultural activities. Concurrently, the drivers of land scarcity uniquely affect agricultural viability: urbanization transforms arable land into urban areas, population growth amplifies competition for the remaining land resources, and desertification degrades soil quality due to unsustainable land-use practices (Al-Mulali and Che Sab, 2018; Sulemana and Machol, 2023).

Given the critical role that agriculture plays in many developing economies, particularly in Africa—where it contributes around 14% to GDP and employs nearly 53% of the workforce—finding sustainable solutions is essential (Painter et al., 2022). Estimates indicate that sustainable agricultural practices must facilitate a 70% increase in global food production by 2050 to meet the demands of a population projected to reach nine billion people (Khandelwal et al., 2022; Sulemana and Machol, 2023). Thus, effectively addressing the challenges posed by climate change is vital for enhancing agricultural productivity and ensuring food security for the growing global population.

The continuous improvement in agricultural production has played a significant role in shaping human history. As the global population continues to grow, the adoption of sustainable agrifood systems is crucial for ensuring food security and achieving Sustainable Development Goal 2 (SDG 2). To achieve this, key improvements in the agricultural sector are necessary, including transitioning to more productive environments, enhancing agricultural management practices, selecting superior seeds or breeds, and adopting innovative production techniques that leverage genetic advancements (FAO, 2022). Recent insights into molecular genetics have further accelerated crop and animal improvements, significantly amplifying production capabilities. Among the innovative agricultural tools emerging today, genome editing (GEd) stands out due to its ability to enhance plant and animal genetics in ways that directly improve food security. When compared to traditional breeding methods, genome editing is more efficient and precise, significantly reducing the time needed to develop new crop varieties or animal breeds while allowing for targeted alterations in genetic make-up. The application of GEd can enhance the resistance of crops and animals to pests and diseases, improve nutritional content, shorten production cycles, and bolster resilience to abiotic stresses induced by climate change, thus exemplifying the potential of advanced agricultural technologies in supporting global food security.

However, these new agricultural innovations, notably involving genome editing and genetically modified organisms (GMOs), are subject to both international and domestic regulations. Member States of the African Union are encouraged to create regulatory frameworks governing these new genomic technologies and their applications. Such regulations must ensure the safe and sustainable utilization of innovations aimed at enhancing food security. Currently, the development, implementation, and enforcement of these regulatory frameworks vary significantly across countries, with some nations having more advanced policies, legislations, and guidelines in place than others (Masehela and Barros, 2023). Hence, the aim of this review is to explore the genome editing policy landscape in Africa, focusing on key countries such as Kenya, Nigeria, Malawi, Ghana, Mozambique, and Burkina Faso. These nations are not only developing but are also finalizing guidelines for the application of emerging genomic technologies. By examining the regulatory frameworks in these countries, this paper highlights how flexible and adaptive policies can encourage bio-innovation while simultaneously addressing socio-economic and environmental challenges.

2 Context and background

2.1 Agricultural biotechnology in Africa

Empirical evidence unequivocally demonstrates that agricultural innovations are essential in addressing the complex challenges that

hinder food security. In this context, Africa has made significant strides in adopting agricultural biotechnologies to enhance crop production. The continent has utilized various plant biotechnology tools, including traditional methods such as hybrid technology, plant tissue culture, micropropagation, and molecular marker-assisted breeding (Akinbo, 2008; Akinbo et al., 2007; Akinbo et al., 2010). One notable example is the use of hybrid technology to improve agricultural production in Africa, which dates back to the early 1980s. Egypt pioneered local hybrid rice varieties in collaboration with the International Rice Research Institute (IRRI) (El-Mowafi et al., 2009; El-Mowafi et al., 2019). This initiative led to the development of 50 local hybrids by the African Rice Center by 2000, culminating in the commercialization of ISRIZ09 in Senegal in 2017. The African Agriculture and Technology Foundation (AATF) has also played a crucial role in developing and testing two-line rice hybrids across the continent, partnering with IRRI through the Alliance for Hybrid Rice in Africa to enhance adoption and capacity building (El-Namaky and Demont, 2013; Abebrese and Yeboah, 2020). In addition to rice, other crops have benefited from hybrid technology. For instance, South Africa introduced hybrid maize in 1949 (Fischer, 2022), leading to extensive collaboration among organizations such as CIMMYT and AATF, as well as national agricultural research institutions and seed companies, to develop and distribute hybrid maize effectively to farmers.

While maize hybrids have gained significant traction due to their staple crop status, both public and private sectors have also produced hybrid varieties of diverse crops, including lettuce, broccoli, eggplant, strawberries, and citrus fruits, which demonstrate increased resilience to environmental stresses. In parallel with hybrid technology, other biotechnology tools have emerged as essential components of Africa's agricultural innovation landscape. Plant tissue culture, for example, has facilitated the growth and dissemination of disease-free plant materials, enhanced the production of secondary metabolites, and allowed for the cultivation of various crop species in bioreactors (Brink et al., 1998; Moyo et al., 2011). Furthermore, molecular marker breeding tools have revolutionized the development of new plant varieties, reducing the commercialization timeline from an average of 10–25 years to merely 7–10 years (Akinbo et al., 2012; Okogbenin et al., 2012). The availability of publicly accessible plant genome sequences has fostered the successful application of this technology, which is grounded in the understanding that an organism's DNA encodes its phenotypes. Across Africa, researchers have employed molecular markers to tackle challenges such as resistance to bacterial blight, enhanced vitamin content, and submergence tolerance in crops (Verdier et al., 2012; Oladosu et al., 2020; Datta et al., 2021). Additionally, these markers have proved invaluable for screening progeny for diversity, developing resistant and tolerant varieties, and creating germplasm for research purposes, thus improving the efficiency and effectiveness of plant breeding programs across Africa (Olasanmi et al., 2021; Conde et al., 2024). As Africa continues to navigate the complex challenges of food security, there are substantial opportunities to enhance resilience through innovative solutions, particularly as genetic engineering and genome editing technologies gain momentum in the region.

2.2 Genetic engineering

Forty-eight countries in Africa have signed the Cartagena Protocol on Biosafety (CPB), reflecting a significant commitment to enhancing biosafety regulations. However, there's a notable disparity between commitment and implementation, as only about a dozen countries have functional biosafety systems in place, with Rwanda being the latest to join the ranks (Mackenzie et al., 2003; Timpo, 2019; Nduwumuremyi, 2024). This gap underscores the need for sustained support and development of biosafety infrastructure across the continent. In terms of genetically modified (GM) crop commercialization, South Africa is leading the charge, with a substantial number of approved GM crops and acreage under cultivation. Other countries, including Kenya, Nigeria, and Ghana, have also begun to approve various GM crops for commercial production, indicating a growing acceptance of this technology (Gbadegesin et al., 2022).

To tackle the challenges associated with the adoption of GM crops, several organizations, including AUDA-NEPAD and ISAAA, are actively working to increase the number of functional biosafety systems. Their initiatives focus on harmonizing regulations governing GM trade and research while ensuring the protection of human, animal, and environmental health. As a result, these efforts aim to facilitate the responsible adoption of GMOs, which is gaining momentum across Africa. Key stakeholders such as the AUDA-NEPAD African Biosafety Network of Expertise (AUDA-NEPAD ABNE), the African Agriculture Technology Foundation (AATF), and National Agricultural Research Organizations (NAROs) have forged successful collaborations aimed at addressing the pressing challenges faced by small-scale farmers. These challenges include issues related to low yields, environmental safety concerns, and the need for skills transfer to utilize innovative products effectively (Gbadegesin et al., 2022; ABNE, 2017). Through these initiatives, the collaborative efforts of these organizations contribute to a more sustainable and productive agricultural sector in Africa, supporting technology uptake through training and capacity-building programs. By fostering an environment conducive to the responsible adoption of GM crops, these endeavors are poised to enhance food security and agricultural resilience across the continent.

2.3 Genome editing

The fourth platform making a significant impact on African agriculture consists of genome editing tools. As the continent grapples with the pressing need to enhance productivity and sustainably to ensure food and nutritional security, it recognizes the increasing importance of technology in agriculture. This acknowledgment has led to substantial strides in the adoption of genome editing techniques, effectively addressing the challenges posed by climate change and other emerging issues. Among these innovative methods, the CRISPR-Cas9 tool stands out for its extensive application in improving staple food crops. For instance, ongoing improvements are being made in crops such as bananas, with efforts dedicated to developing resistance and enhancing yield against diseases like Xanthomonas Campestris. Additionally, breeding initiatives for maize are actively targeting

resistance to Maize Lethal Necrosis (MLN), which is currently undergoing national performance trials, and sorghum is being bred to resist the Striga parasite. Furthermore, researchers are working on developing herbicide-resistant yam varieties (Akinbo et al., 2021; Kaur et al., 2018; Boddupalli et al., 2020; Tripathi et al., 2022; Adegbaju et al., 2024).

Aligning with this technological shift, the African Union has recognized, in its Agenda 2063, the necessity of adopting and deploying emerging technologies like genome editing to transform the agriculture and food systems sector while simultaneously driving economic development forward. To facilitate this transformation, advisory opinions have been provided to member states through the African Union Panel on Emerging Technologies (APET) (African Union High-Level Panel on Emerging Technologies (APET), 2016). Consequently, countries such as Kenya, Nigeria, Ghana, and Malawi have utilized this advisory to develop science-based policies, creating robust frameworks for the regulation of research and trade in genome-edited products (Runo et al., 2024). The Cartagena Protocol on Biosafety (CPB) (Mackenzie et al., 2003) serves as a guiding global framework under which genome editing guidelines are established within national biosafety frameworks. These four countries undertook the development of their frameworks through broad stakeholder consultation forums, ensuring inclusive participation. Regulatory categorization hinges on whether novel (exogenous) DNA sequences are introduced into an edited product or not. For example, genome-edited organisms developed using the so-called site-directed nuclease (SDN)-1 and -2 mechanisms, which respectively use no-homologous end-joining (NEJ) and homology-directed repair sequences without inserts, are classified as conventional varieties when confirmation is provided that no novel DNA sequences were inserted into the resulting organism. Without such proof, these organisms will be categorized as GMOs. Conversely, products generated using the SDN-3 mechanism are unequivocally GMOs, as this approach, per definition, uses homology-directed repair sequences that include novel sequences/inserts, which are transferred to the edited host organism (Runo et al., 2024). To further promote the benefits of genome editing, AUDA-NEPAD spearheads communication and advocacy activities across eight countries: Kenya, Nigeria, Ghana, Burkina Faso, Mozambique, Malawi, Ethiopia, and Zimbabwe. These initiatives aim to raise awareness of the transformative potential of genome editing tools in achieving sustainable agriculture. The significance of these communications and advocacy efforts cannot be overstated; they serve as critical linchpins, translating scientific innovations into actionable solutions vital for realizing sustainable development not only in agriculture but across other sectors of the economy as well.

2.4 Biodiversity

Agriculture is a vital sector in Africa, contributing significantly to many countries' GDP. To combat climate challenges, African nations have developed adaptive agricultural policies that incorporate biotechnology, alongside partnerships at international and regional levels for over two decades (Rock and Schurman, 2020). As climate change intensifies, prioritizing ecosystem health becomes crucial for human wellbeing, as the sustainability of agriculture is directly linked to the health of our ecosystems (He et al., 2021). Biotechnology and biodiversity play critical roles in addressing pressing global challenges while unlocking new economic opportunities. The conservation of biological diversity is essential for tackling issues such as population growth, soil degradation, and resource depletion (Tripathi et al., 2021). Through innovative applications, biotechnology has not only produced food and medicine but has also provided methods to regulate and enhance efforts aimed at combating biodiversity loss (Olomola et al., 2024).

The Convention on Biological Diversity, enacted in 1992, highlights the global commitment to conserving biodiversity, sustainably using biological resources, and equitably sharing benefits obtained from these resources (IUCN, 1994). Nonetheless, biodiversity loss remains a significant concern, with approximately one-third of plant species currently under threat. The biological diversity of ecosystems serves as the foundation for essential services, including water provision, food supply, and climate regulation. In light of this, many African countries recognize the severe importance of biodiversity and ecosystem services in promoting economic growth, sustainable development, and human welfare (AUDA-NEPAD APET, 2022). For instance, the unique marine ecosystems of the Western Indian Ocean provide local communities with food security, livelihoods, and natural beauty. This emphasizes the urgent need for sustainable management practices to protect these invaluable resources (IUCN, 2021).

However, despite the significance of biodiversity, human activities and climate change have led to substantial biodiversity loss across the continent. Healthy biodiversity and ecological productivity are essential for sustaining local economies and supporting communities (Worm and Lotze, 2021). Furthermore, the adoption of agricultural biotechnology in Africa has been sluggish, hindered by various complex socio-political, regulatory, and business factors (Wise, 2021; Neale et al., 2022). As climate change continues to present challenges, biotechnology emerges as a powerful ally in enhancing biodiversity and maintaining healthy ecosystems. By leveraging innovative biotechnological solutions, African nations can better navigate the complexities of agricultural sustainability and work toward a more sustainable future.

2.5 Challenges: knowledge gaps, technophobia, and inconsistencies with global agreements

Africa has made significant strides in creating an enabling environment for the adoption and deployment of agricultural biotechnologies, which are crucial for transitioning the agriculture and food systems sector toward sustainable pathways. However, several challenges continue to hinder the realization of maximum benefits from these emerging technologies. Foremost among these challenges is public perception, which is often shaped by concerns related to food and nutrition security, population growth, and environmental degradation. The existing knowledge gaps between developers, farmers, and the general public contribute to anxieties and misconceptions that impede the broader adoption of innovative agricultural practices. To tackle these issues,

organizations such as AUDA-NEPAD, AATF, CGIAR, and the FAO emphasize the importance of stakeholder engagement. By fostering a common understanding among all parties involved and obtaining social licenses for biotechnology initiatives, these organizations aim to build trust and transparency. In parallel, it is essential that regulatory frameworks align with global agreements, such as the Cartagena Protocol on Biosafety. While many African countries have signed the protocol, they often struggle with its implementation, which further complicates the landscape for agricultural biotechnology.

In addition to these perception-related challenges, African agriculture faces dwindling public investments in research and development (R&D), with funding averaging only 0.42% of GDP. This is significantly lower than the global average of 1.7% (Adepoju, 2022), which limits the continent's capacity to adequately respond to emerging agricultural challenges. Compounding this issue is weak farmer demand, which is largely a result of subsistence farming models. Addressing this requires targeted communication and advocacy strategies tailored to the needs of farmers and their communities. Furthermore, intellectual property (IP) ownership concerns can hinder the uptake of biotechnology. However, organizations like CGIAR and AATF are bridging this gap by accessing essential tools for the public good. While these initiatives support research and farmer adoption, more work is needed to address the complexities surrounding IP rights and ensure equitable access to biotechnology innovations.

Ultimately, a multi-faceted approach is necessary to overcome these challenges. This approach should encompass robust stakeholder engagement, regulatory harmonization, increased investment in R&D, and strategic communication designed to enhance demand for agricultural innovations. By fostering such an environment, Africa can pave the way for sustainable agricultural development, harnessing the full potential of biotechnologies to ensure food security and resilience against future challenges.

2.6 Continental policies: introduction to CAADP Malabo declaration and CAADP Kampala declaration

The Comprehensive African Agriculture Development Programme (CAADP) was established in 2003 when Heads of State and Government convened in Maputo and signed the Maputo Declaration. This pivotal agreement aimed to enhance agricultural productivity and food security across the African continent, rooted in the recognition that agriculture serves as the backbone of many African economies and is a primary source of livelihood for the majority of its people. To realize this ambitious goal, member states committed to allocating a minimum of 10% of their national income to agriculture, with the objective of achieving at least 6% annual productivity growth (CAADP, 2003).

In a further demonstration of commitment, the goals and targets outlined in the Maputo Declaration were reaffirmed a decade later during the 23rd session of the African Union (AU) assembly in Malabo, Equatorial Guinea. This session not only marked the 10-year anniversary of CAADP but also saw heads of member states reiterate their dedication to the principles and values of the programme. Key commitments made included the urgent aim of ending hunger by 2025, halving poverty through agricultural transformation, enhancing financial investments in agriculture, boosting trade in agricultural commodities among member countries, and improving the resilience of livelihoods against climate-related risks. Additionally, member states underscored the importance of mutual accountability regarding CAADP actions and results, alongside strengthening the AU to effectively support these commitments (CAADP, 2003).

As part of the latest CAADP biennial review, 49 member states submitted their reports to the commission in coordination with Regional Economic Communities (RECs). In this review, the benchmark for a country deemed to be on track rose from an initial score of 3.94 in 2017 to 9.29 for the 2023 evaluation. Alarmingly, however, no country currently meets the commitments set for 2025. This situation highlights the pressing need to accelerate the implementation of initiatives designed to build resilient agricultural systems in line with CAADP's vision. Notably, the overall Africa-wide score for this biennial review stands at 4.56, reflecting an improvement from 4.32 in 2021 and 4.03 in 2019 (African Union Commission, 2024).

These recent developments have catalyzed the urgency to formulate a post-Malabo strategy and action plan for CAADP spanning the next decade (2025–2036). This strategy was reviewed and validated during a meeting in Kampala in August 2024. Notably, this progression aligns seamlessly with the African Common Position established at the UN Food Systems Summit in Ethiopia in February 2024. The Summit called upon the African Union Commission to develop a comprehensive strategy and action plan for the period from 2026 to 2035, which will be deliberated upon by heads of state and anticipated to culminate in the Kampala Declaration set for adoption in January 2025 (African Union, 2024).

3 Selected national policy and regulatory frameworks for genome editing

3.1 Kenya

After signing and ratifying the Cartagena Protocol on Biosafety (CPB) in 2003, Kenya made significant strides in biotechnology by developing and publishing the National Biotechnology Development Policy in 2006. This policy acknowledged the essential role of biotechnology in reducing poverty, improving food security, and conserving biodiversity and the environment. To ensure responsible advancement in the field, the Kenyan government created a biotechnology and biosafety policy, which serves as a strategic guide for the growth and application of biotechnology while safeguarding both citizens and the environment from potential harm. A key commitment of this policy was to conduct and manage risk assessments for all introduced GMOs. The policy also laid the groundwork for developing legislation that would regulate and protect the use of biotechnology products, all while fostering an environment conducive to the advancement and commercialization of biotechnology (National Biotechnology Development Policy, 2006).

In 2009, the Kenyan Parliament responded to the growing need for regulation by enacting the Biosafety Act, which specifically

governs activities related to GMOs. This Act established the National Biosafety Authority (NBA, 2011) as the principal body responsible for coordinating and implementing biotechnology regulations within Kenya. With this legal framework, the NBA acquired the authority to oversee all actions involving GMOs across various sectors, including food, feed, research, industry, trade, and environmental release (Republic of Kenya, Biosafety Act, 2009).

The objectives of the Biosafety Act are multifaceted and aim to facilitate responsible research on GMOs while minimizing potential risks. Key goals include ensuring adequate protection for the safe transfer, handling, and use of GMOs that could impact human health and the environment, as well as establishing a transparent, science-based, and predictable process for reviewing and making decisions regarding various GMO-related activities (Republic of Kenya, Biosafety Act, 2009).

To enhance the regulation of GMOs at different stages of their development and use, four sets of regulations were established. The Biosafety Contained Use Regulations of 2011 guide activities involving GMOs in research settings such as laboratories and confined field trials (CFTs) (NBA-Kenya, 2011a). The Biosafety Environmental Release Regulations of 2011 cover the release of GMOs into the environment, their market placement, and commercialization (NBA-Kenya, 2011b). Additionally, the Biosafety Import, Export, and Transit Regulations of 2011 focus on ensuring the safe movement of GMOs into, within, and out of Kenya (NBA-Kenya, 2011c). Finally, the Biosafety Labeling Regulations of 2012 facilitate the labeling of approved GMO products for marketing (NBA-Kenya, 2012).

To date, the NBA has reviewed and granted approval for over 50 research projects and three environmental release applications. Notably, the environmental release approvals encompass Bt cotton (MON 15985), which is actively cultivated, Bt maize (MON 810), which is awaiting variety release, and virus-resistant cassava (VIRCA), currently undergoing national performance trials (NBA-Kenya, 2024). Unfortunately, these approvals have encountered resistance from various groups, which have led to litigation.

In light of recent advancements in genome editing technology, the NBA has developed guidelines expressly designed to determine the regulatory processes applicable to genome editing techniques and their resulting products. Recognizing that genome editing can produce organisms qualifying as GMOs or those indistinguishable from traditionally bred organisms, the Guidelines for Genome Editing in Kenya stipulate that genetic modifications may also create changes achievable through conventional breeding methods (NBA-Kenya, 2022).

According to the Biosafety Act of 2009, GMOs are classified as organisms possessing a novel combination of genetic material derived from modern biotechnology techniques (Republic of Kenya, Biosafety Act, 2009). This definition harmonizes with the Cartagena Protocol's description of living modified organisms (Secretariat of the Convention on Biological Diversity, 2000). Consequently, it follows that any genome editing product that does not qualify as a GMO must be subjected to a different regulatory pathway (Figure 1). This distinction aligns with the Policy Framework for Applications of Genome Editing in African Agriculture, which advocates for a structured, harmonized, and scientifically sound regulatory system across the continent (AUDA-NEPAD APET, 2022). Such globally harmonized regulations could significantly enhance international trade in agricultural products while ensuring a high level of safety.

The Guidelines for Genome Editing in Kenya incorporate an expedited early consultation process, aligning closely with approaches adopted by numerous other countries (Figure 1). Within this framework, applicants are required to complete the designated Early Consultation Form and submit it to the NBA, supplying detailed information on the experimental procedures and resulting products. This process is applicable to all genome-edited plants, animals, and microorganisms involved in research, environmental release, market placement, import, export, and transit that the applicant seeks to classify as genome-edited organisms. The regulatory pathway is assessed on a case-by-case basis, depending on whether transgenic materials are involved (NBA-Kenya, 2022).

If a genome editing technique or derived product is classified as a GMO, the applicant is instructed to submit a GMO application in the prescribed format. Conversely, if a non-GMO determination is made, ongoing monitoring for unintended effects is mandated for the duration of the approval, adhering to biosafety requirements (NBA-Kenya, 2022).

This distinct regulatory pathway for genome editing not only conserves time and resources but also avoids the lengthy and costly GMO approval process. Currently, the focus has been on less commercially significant crops, such as striga-resistant sorghum, which is subject to field trials. Thus far, the NBA has reviewed seven early consultation applications for field trials (covering maize, sorghum, bacteria, and rice) that received non-GMO determinations. Consequently, regulation of these genome-edited products has transitioned to other relevant regulatory agencies, which are also partner entities of the NBA. Notably, the NBA has yet to receive any applications for the commercialization of genome-edited products.

3.2 Nigeria

Nigeria recognizes the significant potential of modern technologies to enhance food security, mitigate the impacts of climate change, and support economic growth for its rapidly expanding population. To harness these opportunities, Nigeria has implemented policies designed to facilitate research and the commercialization of biotechnology products (Adegbaju et al., 2024). Specifically, the National Biotechnology Policy, introduced in 2015, was established to oversee all activities related to modern biotechnology, including research, development, and commercialization efforts. Despite the acknowledged societal benefits of these biotechnologies, there is a consensus within the international community, including Nigeria, that a balanced and comprehensive approach to biosafety is vital. This approach ensures that effective measures are in place to manage any potential adverse impacts that these products may have on human health and the environment (Adewumi and Ilori, 2019).

From a regulatory perspective, Nigeria employs two key approaches to managing modern biotechnologies: leveraging existing legislation across diverse multi-sectoral agencies, and

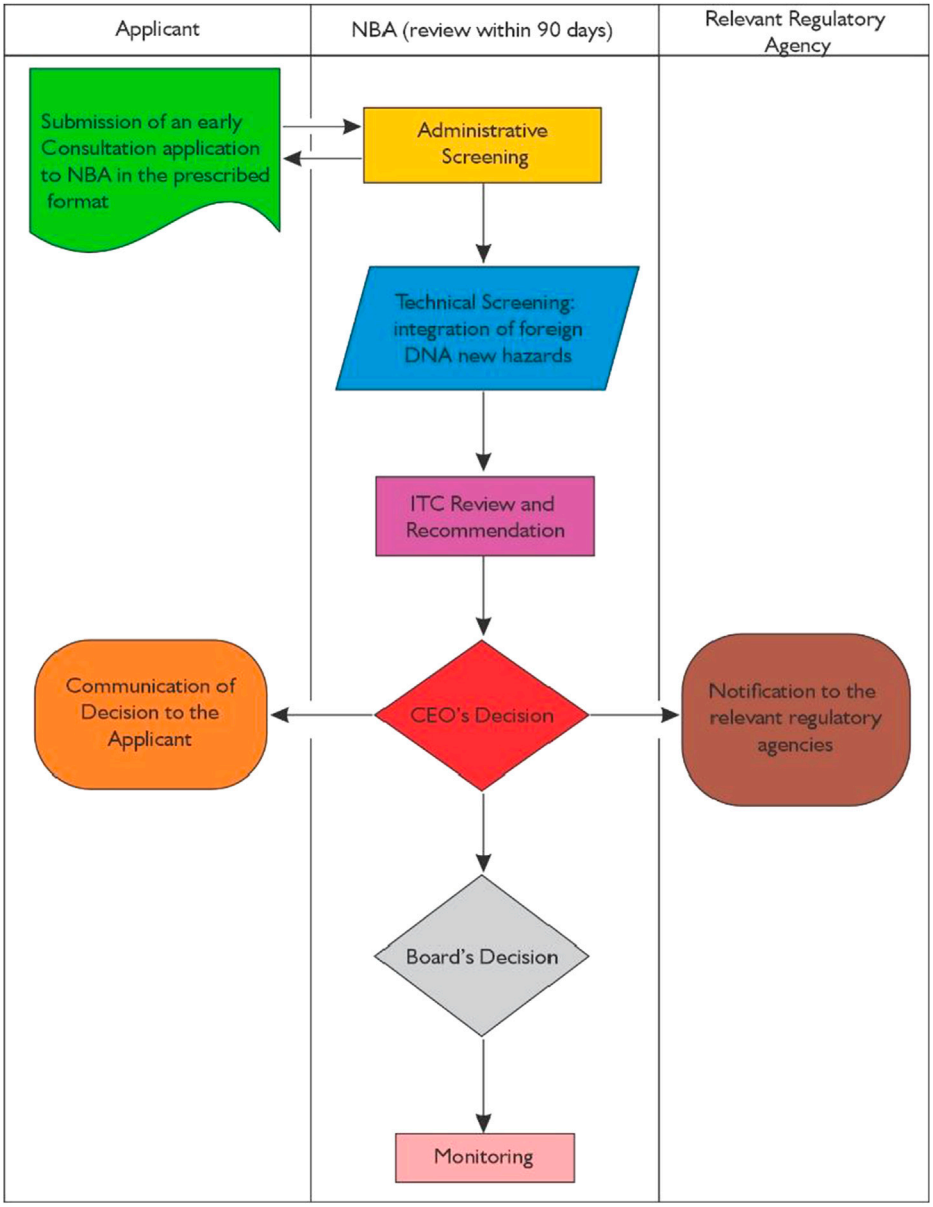

FIGURE 1
Flowchart for the Early Consultation on genome Editing process in Kenya.

creating new biosafety laws with clear legal authority and centralized decision-making bodies (Tachikawa and Matsuo, 2023). Reflecting the common practice among African nations, Nigeria has adopted the latter approach. Furthermore, Nigeria is a signatory to the Convention on Biological Diversity (CBD) and the Cartagena Protocol on Biosafety (CPB), ratified in 1994 and 2003 respectively. These pivotal agreements laid the groundwork for developing a robust national regulatory framework aimed at addressing the potential adverse effects stemming from the transboundary movement, handling, use, and release of GMOs on human health, biodiversity, and the environment. In alignment with these multilateral agreements, the first and second National Biosafety Guidelines were established in 1994 and 2001, respectively, which culminated in the drafting of the National Biosafety Management Agency (NBMA) Bill that was subsequently enacted into law in 2015 (Adewumi and Ilori, 2019; Nwosu and Bello, 2023).

The NBMA (2015) established the National Biosafety Management Agency as the competent national authority overseeing all biosafety matters. The agency is tasked with providing a regulatory framework, along with institutional and administrative mechanisms to ensure safety measures are effectively implemented in the application of modern biotechnology in Nigeria. This framework aims to prevent any adverse effects on human health, biodiversity, and the environment (National Biosafety Management Agency Act, 2015). In 2019, the Act was amended to include provisions for regulating emerging biotechnologies, such as genome editing, gene

drives, and synthetic biology, as well as measures to enhance biosecurity.

Under the NBMA Act of 2015 (as amended), Nigeria regulates several activities related to GMOs, which include contained use, confined/multi-locational field trials, commercialization, and the import and export of GMOs for food, feed, and processing purposes. With socio-economic and ethical considerations integrated into the regulatory process, the legislation emphasizes comprehensive oversight (Adewumi and Ilori, 2019; Nwosu and Bello, 2023). For activities involving contained use and confined field trials, responsible institutions are required to obtain accreditation and have their facilities certified by the NBMA. Additionally, research endeavors in modern biotechnology are supervised by Institutional Biosafety Committees (IBCs) within those institutions, which report directly to the Agency.

Regarding the release of GMOs into the environment—whether for confined or commercial use, or for food, feed, or processing—the NBMA Act mandates a risk assessment review process to be conducted on a case-by-case basis. This review must be transparent and scientifically rigorous, taking into account information provided by the applicant, public opinion, and scientific expertise from the Ad Hoc National Biosafety Committees and the National Biosafety Technical Sub-Committees. Furthermore, available data from reputable sources such as the Biosafety Clearing House (BCH), the Organization for Economic Co-operation and Development (OECD), and the European Food Safety Authority (EFSA) can also inform these assessments.

In a landmark achievement, Nigeria became the first African country to approve the commercialization of a locally developed GM food crop, the Pod-Borer Resistant Cowpea, in 2019. This crop expresses the Cry protein designed to combat the insect pod-borer, Maruca vitrata (Ehirim et al., 2020; Kedisso et al., 2022). Additionally, Nigeria has granted commercialization approvals for other crops, including Bt cotton, which is resistant to bollworms, and TELA maize, which tolerates moderate drought while also resisting the fall armyworm (Spodoptera frugiperda) and stem borers (Nwosu and Bello, 2023).

Moreover, in 2019, Nigeria positioned itself as one of the pioneer nations in Africa by amending its Biosafety Act to accommodate the regulation of emerging biotechnologies (Komen et al., 2020; Adegbaju et al., 2024). The National Guideline on Genome Editing was validated on 19 December 2020, outlining the necessary processes for all dealings related to genome editing within Nigeria, as well as the requirements for applications concerning genome-edited products. These guidelines stipulate that applicants engaging in genome editing or utilizing genome-edited products are required to apply, providing essential information to the National Biotechnology Authority (NBMA), which will ascertain the GMO classification of their product on a case-by-case basis. Despite the regulatory variances, all genome editing processes/products are subject to varying levels of regulatory oversight. If a genome editing process does not result in a new combination of genetic material, it falls under a non-GM regulatory classification that requires a Clearance Permit (Figure 2). Conversely, any process necessitating recombinant DNA or resulting in a new combination of genetic material will categorize the product as a GMO, thus placing it under GM regulations.

In summary, all dealings involving genome editing in Nigeria must secure approval from the NBMA, either through Clearance Permits or Approval Permits, contingent upon the regulatory classification. The agency determines the regulatory pathway

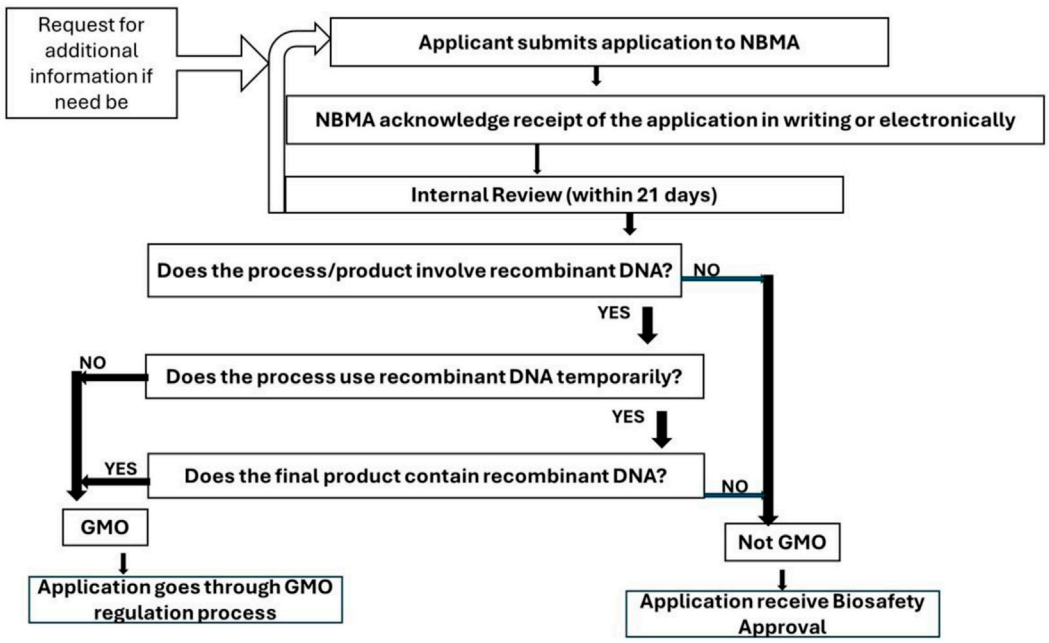

FIGURE 2
Flowchart for the Early Consultation on genome Editing process in Nigeria.

based on an internal review following consultations with the applicant, thereby ensuring a level of accountability and scientific rigor in the management of biotechnology products.

3.3 Ghana

To fully harness the potential of genome editing products, a balanced approach is crucial, one that prioritizes safety, equity, and ethical considerations. Ghana is making strides in this direction, leveraging its well-established and comprehensive regulatory frameworks to advance genome editing technologies. These existing policies not only provide a solid foundation but also facilitate the effective adoption and integration of genome editing technologies within the country. By aligning safety and ethical standards with technological advancements, Ghana aims to ensure that the implementation of genome editing contributes positively to its agricultural and biotechnological landscape.

The Constitution of Ghana establishes a strong foundation for promoting science and technology through education. Specifically, Section 38(3) (a) of the 1992 Constitution mandates the state to ensure access to education at all levels, placing a particular emphasis on science and technology. This provision plays a crucial role in integrating genome editing into educational curricula, equipping students with the knowledge and skills necessary to advance in this rapidly evolving field. By prioritizing science and technology education, Ghana not only fosters a well-informed workforce but also enhances its capacity for innovation. This strategic focus ultimately contributes significantly to national development through the practical applications of genome editing, positioning the country as a leader in biotechnology advancements.

The Biosafety Act 2011 (Act 831) serves as the cornerstone of biotechnology regulation in Ghana, overseeing the safe development, transfer, handling, and use of genetically modified organisms and related technologies, including genome editing. Within this framework, the establishment of the National Biosafety Authority (NBA) plays a critical role in ensuring that genome editing activities are conducted in a safe and regulated environment. To further enhance this regulatory landscape, comprehensive guidelines were introduced in October 2023 under the Biosafety Act. These guidelines provide clear processes for risk assessment, management, and decision-making, effectively addressing legal and policy uncertainties through scientifically sound, case-by-case evaluations. They outline specific criteria to determine whether an organism or product derived from genome editing techniques falls under the regulation of the Biosafety Act. Notably, products resulting from genome editing that do not contain inserted genes or derivatives of foreign genes in the final product are exempt from regulatory control under the Act.

In order to streamline the regulatory process, the NBA encourages applicants to participate in pre-submission consultations. This preliminary step involves completing a pre-submission consultation form, which helps ascertain the regulatory status of the application and provides a systematic approach to ensure predictability in decision-making (Figure 3). Such consultations equip applicants with a thorough understanding of the regulatory requirements and assist in aligning their submissions with the established guidelines, thereby potentially reducing delays in the approval process. Additionally, the regulatory focus centers on the classification of genome-edited products based on whether they contain inserted genes and the nature of these insertions. By employing a case-by-case approach to decision-making, the guidelines allow for flexible and adaptive regulatory measures tailored to the specific applications of genome editing and their potential impacts.

Crucially, the regulatory guidelines for genome editing are designed to be dynamic; they will undergo periodic review and updates in light of new scientific information. This iterative process ensures that the guidelines remain current and relevant, effectively reflecting the latest advancements in genome editing technologies and best practices in biosafety. Through the implementation of these comprehensive guidelines, Ghana significantly strengthens its capacity to manage genome editing technologies responsibly. This fosters an environment that is conducive to innovation while simultaneously ensuring safety and compliance with regulatory standards.

3.4 Burkina Faso

Burkina Faso established a regulatory framework for products derived from modern biotechnology in 2004, starting with a pivotal decree (No. 2004–262/PRES/PM/MECV/MAHRH/MS) adopted on 18 June 2004, which outlined safety protocols for biotechnological applications. In alignment with this decree, the government created the National Biosafety Agency (ANB) in 2005 as the competent national authority to oversee biosafety in the country. The government established the ANB alongside two advisory bodies, which play critical roles in the regulatory process. The first is the National Scientific Committee on Biosafety, tasked with assessing applications related to GMOs and conducting risk evaluations. The second body is the National Biosafety Observatory, responsible for public education, awareness, and monitoring to prevent potential harm. The initial framework facilitated Burkina Faso's first authorization request in 2005 for confined environmental experimentation with Bt cotton (Bollgard II), designed to resist the insect pest *Helicoverpa armigera*. The regulatory evolution continued with the passage of an initial biosafety law in 2006. Lawmakers revised this law in 2012 to address compensation and liability aspects, following Ghana's adoption of the Nagoya-Kuala Lumpur Supplementary Protocol in 2010.

From 2005 to the present day, the ANB has been actively involved in reviewing and granting authorizations for various biotechnological experiments, including contained and controlled environment studies and environmental releases. Key projects within this framework have focused on developing genetically modified crops, including herbicide-tolerant Bt cotton, insect-resistant maize, and cowpeas resistant to pod borers. Additionally, researchers have worked on genetically modified mosquitoes and rice with built-in resistance to bacterial blight. Scientists used CRISPR/Cas9 gene editing to create a new product. They removed and replaced specific genetic material that help produce sugar, which is essential for the growth of the Xanthomonas oryzae bacterium. The dossier for this novel rice variety underwent thorough analysis by the National Biosafety

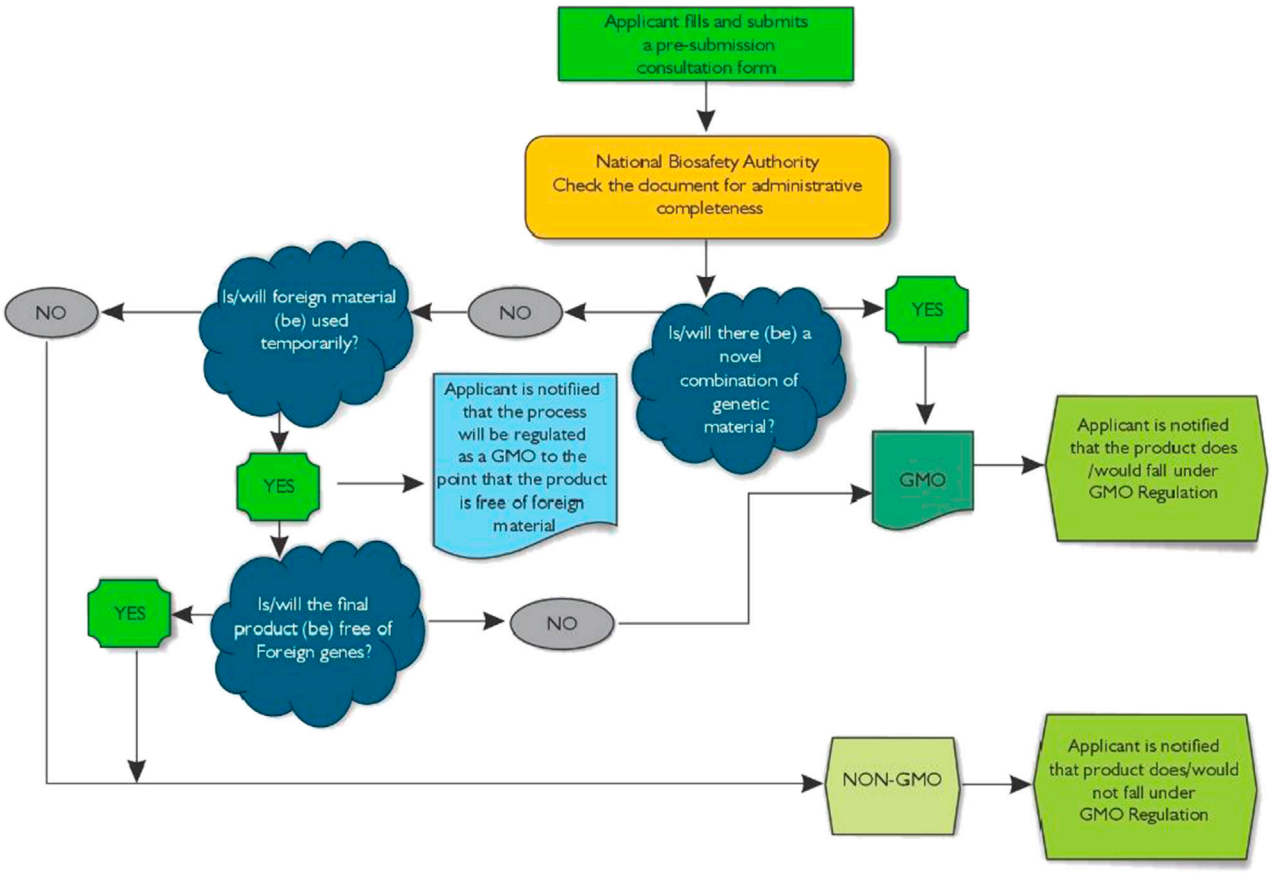

FIGURE 3
Flowchart for the Early Consultation on genome Editing process in Ghana.

Agency, including risk assessments and management measure evaluations, in accordance with existing regulations, before receiving authorization for greenhouse experimentation for a duration of 2 years.

However, the review of the edited rice dossier underscored the necessity for adapting and revising the existing regulations in Burkina Faso. Notably, the absence of a transgene or a new genetic combination in the edited rice suggests a lower risk profile compared to conventional GMOs. Consequently, in 2023, the ANB initiated a comprehensive review of its regulatory practices and created a technical guide to modern biotechnology regulations, particularly focusing on genome editing (Figure 4). This guide delineates the types of organisms and products that are subject to regulation as well as those exempted by law and treated as conventional varieties or breeds. The ANB will exempt genetically modified organisms from regulation under Biosafety Law 064-2012/AN if they meet two conditions. First, the ANB must verify that the final product contains no foreign genes. Second, the organisms must not combine genes from incompatible species.

This adoption of the technical guide enabled the National Biosafety Agency to issue Decision No. 2023-000122/MESRI/SG/ANB/DG on 21 July 2024, authorizing the use of edited rice lines to combat bacterial blight in rice. After securing approval, the farm took a major step forward by testing the genetically edited rice during the 2023–2024 crop year, demonstrating the practical application of biotechnology in Burkina Faso's agricultural sector.

3.5 Malawi

Malawi's economy is predominantly agro-based, with agriculture contributing approximately 30% to the gross domestic product (GDP) and employing more than 80% of the population (NSO, 2019). Recognizing the essential role of innovations and technologies, including biotechnology, in enhancing agricultural productivity, the country seeks to fulfill its aspirations as outlined in the Malawi 2063 development plan. To achieve these goals, Malawi has established mechanisms to ensure that biotechnology is effectively regulated, prioritizing the safety of both the environment and human health. Central to this regulatory framework is the country's comprehensive biosafety legal structure that governs biotechnology activities. Among these foundational regulations is the Biotechnology and Biosafety Policy of 2008, along with the Biosafety Act of 2002 and the Biosafety Regulations of 2007, which specifically address the management of GMOs. Between 2001 and 2002, genetically modified maize in food donations to Malawi triggered a food

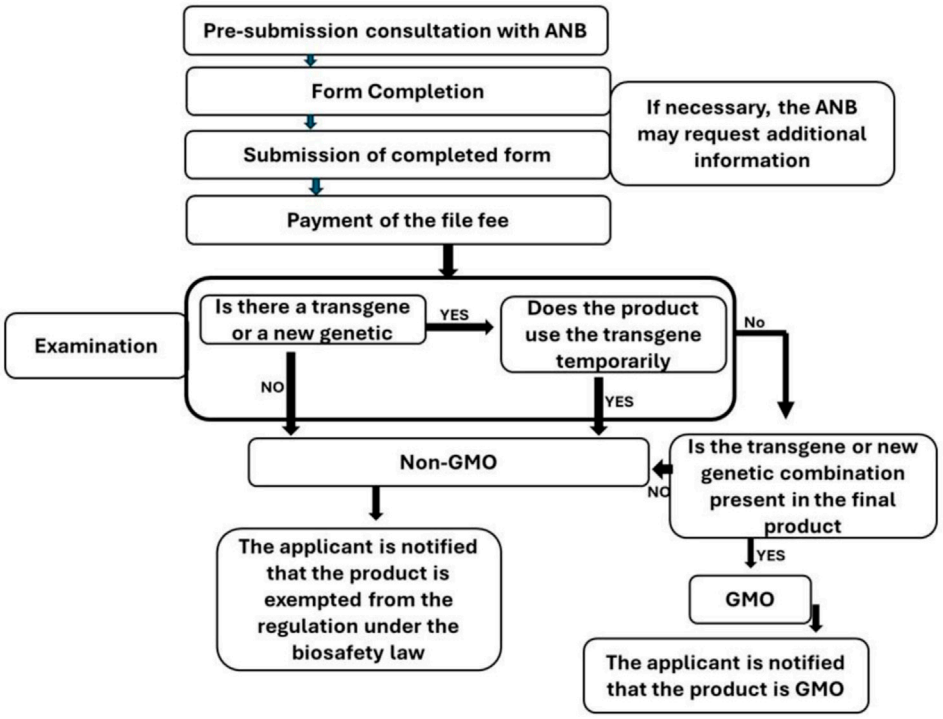

FIGURE 4
Flowchart for the Early Consultation on genome Editing process in Burkina Faso.

crisis, which in turn underscored the need for a robust biosafety framework. In response to this pressing issue, the government expedited the development of its legal framework to ensure the appropriate regulation of future GMOs entering the country.

Further demonstrating its commitment to biosafety, Malawi became a party to the Cartagena Protocol on Biosafety in 2009. Authorities developed guidance documents to complement this step, facilitating effective implementation of the Protocol and national biosafety laws. These documents include guidelines for conducting confined field trials and multi-location trials, guidelines for GMOs with stacked genes, guidelines for safety assessments for food and feed derived from genetically modified crops, as well as guidelines for determining the regulatory processes for genome-edited plants and their products. Although the current laws do not specifically address genome editing, these guidelines provide a framework for regulating genome-edited crops. The Genome Editing (GEd) Guidelines classify products resulting from genome editing as conventional if they do not contain recombinant DNA. In contrast, the guidelines regulate products with transgenes in the same way as other GMOs under the Biosafety law (Figure 5). Regulators thoroughly investigate product development to detect the use of transgenes and their presence in the final product, underscoring the product-based regulatory approach. A flowchart illustrates the steps followed in the regulation of genome-edited products, highlighting the thorough assessments mandated by the guidelines.

Building on this regulatory framework, the National Biosafety Regulatory Committee, established under the Biosafety Regulations of 2007, reviews all biotechnology applications, including those related to genome editing activities, and makes recommendations to the Minister responsible for the Environment for approval. Although Malawi has not yet received any applications for the development or importation of genome-edited products, the country is taking proactive steps to promote genome editing. Two experts from local universities have taken the initiative to undergo training in genome editing techniques. Furthermore, Malawi collaborates with AUDA-NEPAD to spearhead a genome editing project, raising awareness about the benefits of genome editing in combating hunger and achieving the goals of Agenda 2063, the Africa We Want.

3.6 Mozambique

Mozambique's government prioritizes agriculture in its Five-Year Program, using it as a guiding framework to shape national policy. The government makes this a top priority due to several compelling factors: nearly 70% of Mozambicans depend on farming for their livelihoods, and the sector generates around 26% of the country's GDP. Given these significant statistics, any initiatives aimed at supporting and accelerating agricultural development are crucial for Mozambique, particularly amidst growing population pressures and the challenges posed by climate change (Arndt et al., 2010). Smallholder farms dominate Mozambique's agricultural landscape, with commercial farming operations playing a relatively minor role. Unfortunately, the country's agricultural productivity ranks among the lowest in the world (Nhantumbo et al., 2021). To address this issue, sustainable management of natural

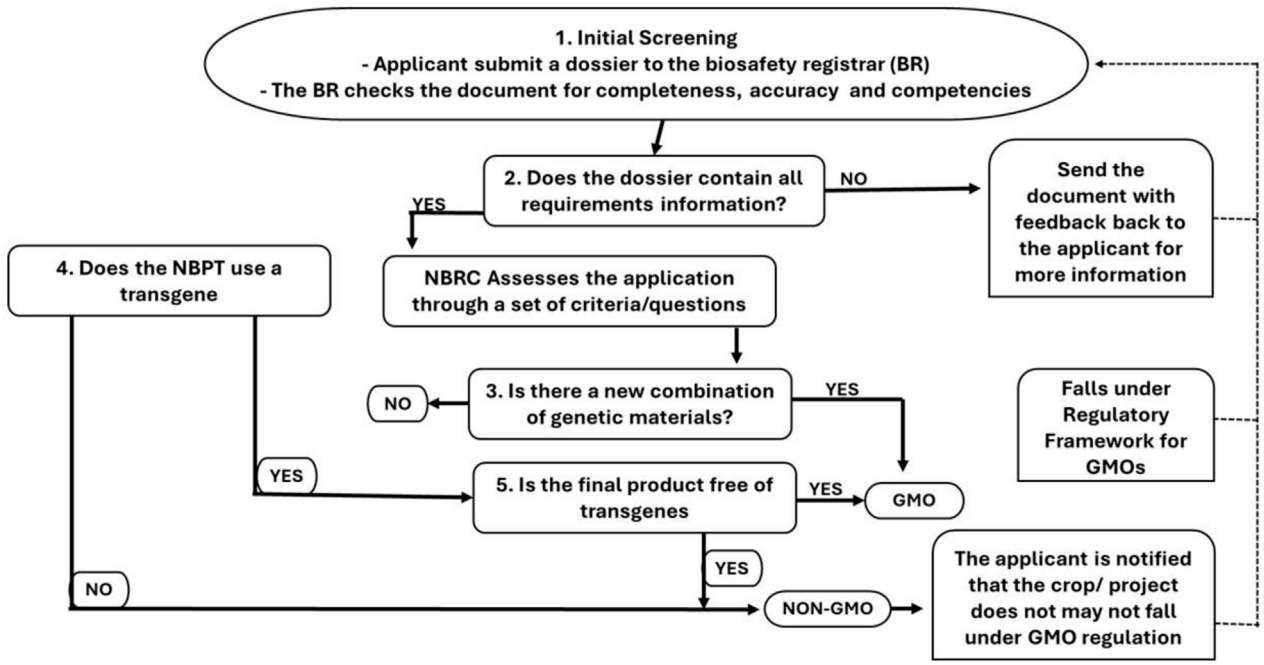

FIGURE 5
Flowchart for the Early Consultation on genome Editing process in Malawi.

resources while simultaneously boosting agricultural production and productivity is essential. The National Strategy for Science, Technology, and Innovation (ENCTI) emphasizes that solid research must guide these efforts. By aligning agricultural development with scientific research and innovation, Mozambique can promote sustainable practices that not only increase output but also ensure long-term environmental preservation.

Researchers in Mozambique actively explore ways to enhance agricultural practices, applying various biotechnological tools and techniques to drive innovation. Initiatives aimed at boosting production, productivity, and addressing both biotic and abiotic stressors are particularly critical given the global advances in biotechnology that have transformed agricultural practices worldwide. Specifically, the application of biotechnology in Mozambique's agricultural sector presents opportunities for improved yields, pest and disease resistance, and enhanced nutrient content in food crops. These advancements are vital for ensuring food security and improving livelihoods across the nation. Innovations in areas such as genetic engineering, precision farming, and soil microbiology hold immense potential for revolutionizing Mozambique's agricultural landscape and contributing to the country's broader sustainable development goals (Nhantumbo et al., 2021; Rooyen and Sigwele, 1998).

Significantly, across the African continent, substantial efforts are underway to adopt modern biotechnology, particularly genome editing. The Centre of Excellence in Science, Technology, and Innovation (CoE STI) established by AUDA-NEPAD is at the forefront of these initiatives. By building strategic partnerships, the center integrates innovations that bridge science and practical application, and spearheads a project to boost agricultural production in Africa. This initiative is part of broader efforts to harness the potential of modern biotechnology, driving industrial growth and fostering inclusive development to accelerate Africa's socio-economic transformation (Thomson, 2007; Itam et al., 2023; Ochieng and Ananga, 2019).

Mozambique draws inspiration from Africa's successful applications of modern biotechnology, particularly genome editing in agriculture, and actively participates in the CoE STI initiative led by AUDA-NEPAD. This initiative emphasizes leveraging genome editing technology to enhance staple food species, including maize, cassava, sorghum, wheat, yams, chickens, and cattle. Through this engagement, Mozambique aims to harness these technologies to improve its agricultural productivity and sustainability (AUDA-NEPAD, 2023; Ku and Ha, 2020). By participating in genome editing initiatives, Mozambique aspires to bolster national expertise among a diverse array of stakeholders, including policymakers, regulators, researchers, and the general public. Policymakers and educators are joining forces to build a skilled and informed workforce. Additionally, Mozambique plans to prioritize research and development focused on species where genome editing can facilitate tailored breeding programs to address their specific production needs.

Moreover, Mozambique perceives these continental and global initiatives as opportunities to enhance its research and development infrastructure and integrate itself into networks of modern biotechnology practitioners, particularly in genome editing. To further demonstrate its commitment to genome editing (GEd) technology, the country has developed and validated a

Communication and Advocacy Strategy. The government implements this strategy to effectively communicate and advocate for genome editing technology among various stakeholders, and executes an action plan that outlines concrete steps and activities to enhance understanding and awareness.

Mozambique has made significant progress in adopting genome editing technology. The government has established guidelines for GEd use and approved a plan to edit specific genes in sorghum bicolor, enhancing light absorption and boosting crop density. However, despite these notable strides, there remains a need for strengthening regulatory frameworks and institutional capacity to ensure the responsible and effective deployment of genome editing and other biotechnologies within Mozambique's agricultural sector (Ku and Ha, 2020; Entine et al., 2021).

4 SWOT analysis of genome editing in African agriculture

Amidst the pressing challenges of food insecurity, climate change, and rapid population growth, African nations are increasingly turning to innovative solutions to boost agricultural productivity. Biotechnology has yielded two prominent categories of products: GMOs and (GEd) products. As the distinction between GEd and GMOs becomes a critical point of debate, a comprehensive SWOT analysis is essential. This analysis dissects the strengths, weaknesses, opportunities, and threats associated with genome editing, providing a nuanced comparison with GMOs. By doing so, it informs evidence-based policy-making and agricultural strategies tailored to Africa's unique challenges. Furthermore, this analysis enables a more effective assessment of the overall value and impact of these techniques (Gudanowska, 2014).

Genome editing boasts several distinctive advantages that underscore its potential to revolutionize agricultural innovation. One of the main advantages of genome editing is its precision, allowing scientists to make targeted changes at specific locations in the genome. This reduces the chance of unintended effects, making it a more appealing choice for improving specific traits. This precision also leads to greater efficiency, as genome editing speeds up the development of crop varieties. Researchers can create improved strains much faster than with traditional breeding methods or genetically modified approaches. When genome editing introduces changes similar to natural mutations, confined to endogenous traits, it mimics the natural process of mutation, yielding a comparable risk profile. This similarity underpins the rationale for distinct regulatory approaches, differing from those applied to GMOs. Consequently, genome editing often faces fewer regulatory hurdles, especially in regions like Africa, where it's perceived as less intrusive (Wolt et al., 2016). This reduced regulatory burden, combined with its inherent biological similarities to natural mutations, can improve public acceptance and simplify approval processes, particularly when compared to transgenic GMOs (Enfissi et al., 2021).

This perspective helps hasten the development and commercialization of innovative crop varieties.

When evaluating genome editing, it is essential to weigh its numerous benefits against several notable weaknesses, particularly those that distinguish it from GMOs. One key limitation is the relatively limited understanding and experience with genome editing in agriculture. Although this technology has substantial potential, it is still emerging compared to the long-established history of GMOs. This newness may cause hesitance among stakeholders because of a lack of long-term data and potential challenges related to implementation. In addition, genome editing technologies tend to be technically complex and often require specialized tools and conditions that are not readily available in many African countries. Furthermore, intellectual property concerns regarding specific genome editing technologies can limit access, hindering their adoption in developing countries due to high costs or restrictive licensing agreements. To address these challenges, African governments should adopt a multi-faceted approach. This includes strengthening STEM education infrastructure and human capital, fostering international collaborations, and developing supportive policies for genome editing technologies. By doing so, research institutions will be empowered to conduct independent, Africa-based research, tackling food security issues. Additionally, establishing Technology Transfer Offices and Intellectual Property Offices within institutions will promote scientific innovation, protect scientists' interests, and maximize the benefits of genome-edited products.

Realizing the potential of genome editing in African agriculture presents numerous opportunities for transformative impact. By enhancing crop yield and resilience, genome editing can play a vital role in boosting agricultural productivity. This technology enables the development of crop varieties that can withstand pests, diseases, and climatic stresses, significantly increasing food production and addressing food insecurity across the continent.

Moreover, countries like Nigeria, Malawi, Kenya, and Ghana are making significant strides by adopting a case-by-case regulatory approach to genome-edited products. This allows certain genome-edited varieties not to be classified as GMOs, thus streamlining the approval process and facilitating quicker access to innovative technologies. By promoting flexible regulatory environments, these countries can encourage research, development, and eventual commercialization of crop varieties tailored to the specific needs and challenges of local farmers.

Additionally, improved crop varieties can empower smallholder farmers by providing them with tools to increase profitability and reduce their vulnerability to climate fluctuations. This empowerment not only augments individual livelihoods but also stimulates economic growth within rural communities. By supporting smallholder farmers, genome editing can play a crucial role in achieving broader national and regional food security goals. Ultimately, embracing genome editing technologies fosters a collaborative environment, enabling African countries, researchers, and institutions to pool resources and knowledge. This cooperation enhances their ability to tackle common agricultural challenges more effectively and drives collective progress across the continent. By taking advantage of innovations in genome editing, African nations can position themselves at the forefront of agricultural technology, ensuring a sustainable and food-secure future for generations to come.

Genome editing's potential is hindered by significant challenges, including consumer skepticism toward biotechnologies. Concerns about safety, ethics, and long-term impacts can impede acceptance of genome-edited crops, echoing the public trust issues faced by GMOs. In South Africa, the regulatory landscape poses a critical threat by categorizing genome-edited products under existing GMO regulations. This classification may intensify public scrutiny, influencing perceptions and regulatory attitudes. Consequently, South Africa's regulatory stance on genome editing will have a ripple effect, serving as a potential blueprint for several African countries and shaping the continent's approach to this technology. This influence extends to regional trade dynamics, consumer perceptions, and agricultural innovation. A fragmented market may emerge across Africa, with varying degrees of acceptance and regulation. Negative consumer reactions in South Africa could encourage skepticism in neighboring countries, heightening fears and resistance. Furthermore, ecological risks associated with genome-edited crops, such as crossbreeding affecting regional biodiversity, and transcend borders. Economically, South Africa's regulatory decisions could impede biotechnology progress in agriculture across the continent, threatening potential advancements. While South Africa, as a sovereign state, has the right to make its own regulatory decisions, other African countries must also be empowered to develop and implement genome editing regulations that are tailored to their unique contexts and needs, based on independent and evidence-based decision-making. Regional bodies like the AU can facilitate this process by promoting regional cooperation and intensify information-sharing, and capacity-building on genome editing. This can include supporting country-led research initiatives, providing access to unbiased scientific expertise, and fostering inclusive dialogues that consider diverse perspectives. By adopting a collaborative and evidence-based approach, several African countries can harness the potential of genome editing while minimizing its risks and tailoring its applications to their specific development priorities.

5 Recommendations

Africa's evolving agricultural technology landscape presents a crucial opportunity for researchers, policymakers, and stakeholders to glean actionable insights. To catalyze effective bio-innovation, particularly in the realm of genome editing, a holistic strategy is paramount. This necessitates a balanced evaluation encompassing innovation potential, socioeconomic implications, and the existing regulatory architecture, thereby establishing a robust foundation for sustainable agricultural practices. Our exhaustive analysis of Africa's genome editing policy landscape, covering key countries such as Kenya, Nigeria, Malawi, Ghana, Mozambique, and Burkina Faso, yields pivotal recommendations to catalyze agricultural innovation via biotechnology.

Firstly, harmonizing policies and aligning national regulations with established continental frameworks, such as the CAADP, is very crucial. This strategic alignment fosters a cohesive regulatory environment, thereby promoting advancements in genome editing and facilitating broader technology adoption across the continent. To address existing knowledge deficits and mitigate technophobia surrounding genome editing, comprehensive education and outreach initiatives are indispensable. Implementing robust educational frameworks will empower diverse stakeholders by demystifying these technologies, facilitating informed dialogue, and promoting active engagement. This, in turn, creates a climate of trust and understanding. Regulatory flexibility is equally crucial. Advocating for adaptive regulatory frameworks that promote sustainable innovation will facilitate the rapid deployment and seamless integration of genome editing solutions into agricultural practices while ensuring adherence to stringent safety and sustainability standards.

Regional cooperation and collaborative partnerships among African nations are vital for the development of standardized policies tailored to unique agricultural contexts, ensuring consistency across borders. Effective monitoring mechanisms should be implemented to continuously evaluate the socioeconomic impacts of genome editing technologies. Strategic investments in capacity-building initiatives will enhance the comprehension and effective implementation of genome editing regulations among policymakers, scientists, and industry stakeholders. Prioritizing robust stakeholder engagement will foster continuous dialogue, address pertinent concerns, cultivate trust, and ensure that policies reflect diverse perspectives. Ultimately, a multidisciplinary approach that effectively integrates next-generation genome editing technologies is vital for addressing food insecurity and overcoming the multifaceted agricultural challenges confronting Africa. By strategically adopting these recommendations, African nations can effectively spearhead agricultural innovation, harnessing the transformative potential of genome editing technologies to secure a sustainable and food-secure future for the continent.

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EDITED BY
Clara Rubinstein,
Institute for Scientific Cooperation in Environment and Health (ICCAS), Argentina

REVIEWED BY
Marcia O. M. A. José,
Bayer, Brazil
Andrea Wilcks,
University of Copenhagen, Denmark

*CORRESPONDENCE
Amy L. Klocko,
aklocko2@uccs.edu

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Mini review: Apple improvement, traditional approaches, biotechnology options, and regulatory considerations

Amy L. Klocko*

Department of Biology, University of Colorado Colorado Springs, Colorado Springs, CO, United States

Apples are a popular and globally important crop. The fruits are eaten fresh, pressed for juice, fermented as cider, processed into sauce, dried, and more. There are thousands of different cultivars, a small subset of which are grown on a commercial scale. Genetic analysis has shown that, as a group, domestic apples have a complicated genetic background, with contributions from multiple wild species. By contrast, most of the highly produced commercialized modern cultivars share a narrow range of genetic diversity. However, as apples are outcrossing, propagated vegetatively, and long-lived, wild and heirloom varieties can be maintained and are valuable sources of genetic diversity for desirable traits. Apples are also amenable to genetic transformation, and work in this area has resulted in improved resistance to diseases and a commercialized non-browning variety, the Arctic™ Apple. Traditional breeding, breeding guided by modern genetic knowledge, and biotechnology all contribute to the overall process of apple cultivar development and represent an important example of how many approaches can be used in crop improvement. As global biosafety regulations continue to develop and change, countries will be tasked with developing guidelines for both the creation and import of apple trees and apple products.

KEYWORDS

apple, biotechnology, germplast, breeding, GMO, apple scab, fire blight

1 Introduction

Malus x *domestica* Borkh. (domestic apple, hereafter apple) is a staple fruit crop grown in many regions of the world. In 2023, over 661,000 ha of apple trees were harvested, mostly in China, India, and Russia, with over 90 countries reporting output (FAO, 2023).

In general, apples are considered either dessert or cider, with the latter being used for the brewing of fermented alcoholic cider. Dessert apples are intended for the fresh fruit market, and are also processed into juice, vinegar, applesauce, dried fruit, and more (Downing, 1989; Guine et al., 2021). Dessert apple juice can be consumed fresh, or fermented into cider, but this approach is aimed at meeting rising consumer as cider cultivars are less commonly grown than dessert varieties (Soomro et al., 2022). By contrast, traditional cider apples are not meant for fresh consumption and are sometimes referred to as "spitters" due to their high phenolic content and rather unpalatable fruits (Marks et al., 2007).

2 Genetics and domestication

Domestic apple was one of the earlier plant genomes to be sequenced, with the first genome version published in 2010 (Velasco et al., 2010). Apples were domesticated in Asia, and genetic analysis of wild and domestic varieties shows evidence of breeding with local wild species in both Asia and Europe as varieties were developed (Cornille et al., 2014; Chen et al., 2023). Many countries have bred locally important varieties of apples, and there is interest in preserving these heritage varieties (see Supplementary Table S1 and examples therein).

Of the over 7,000 domestic apple cultivars, nearly all commercial production is from just a handful of varieties, which share a lot of common genetic heritage (Noiton and Alspach, 1996; Forsline et al., 2003; Pereira-Lorenzo et al., 2018). This lack of diversity in existing elite cultivars adds to the challenge of apple improvement. In general, domestic apple trees are outcrossing, and varieties of interest are maintained by vegetative propagation, often involving grafting a long-established practice (Cornille et al., 2014; Pereira-Lorenzo et al., 2018). As these trees can also be long lived, very old varieties can still be found in modern times. In addition, many wild varieties of *Malus* are compatible with domestic trees, providing an important resource for key traits (Cornille et al., 2014).

2.1 Select apple traits of interest

Like crops in general, apple trees are vulnerable to pathogens, which cause significant economic losses. These include the fungus *Venturia inaequalis* which causes apple scab, *Erwinia amylovora*, causing fire blight, *Penicillium expansum* leading to postharvest disease, and more (MacHardy, 1996; Malnoy et al., 2012; Luciano-Rosario et al., 2020). In general, highly produced commercial cultivars exhibit little to no resistance to those three diseases, which are managed through cultivation practices (Gessler et al., 2006; Holb, 2007; Kellerhals et al., 2012; Luciano-Rosario et al., 2020). Similarly, post-harvest losses from fungal growth can be considerable, with little genetic resistance, fungicides re the typical control method (Gupta and Saxena, 2023). There is great interest in identifying or developing disease resistant cultivars.

In addition to disease resistance, interesting marketable fruit traits are sought after, such as red fleshed fruits, tiny fruits, large sized fruits, or early ripening (Janick et al., 1996; Volz et al., 2009). Other preferred characteristics of fresh market apples such as fruit color, pattern, and texture are variable by region and across time (Janick et al., 1996). As apples intended for the fresh fruit market can undergo extensive storage to allow year-round sales of this seasonal fruit, longer shelf-life is a valuable trait (Janick et al., 1996). Consumers are also interested in obtaining nutritious foods (Rahman et al., 2021). Apples are high in a variety of compounds, including ascorbic acid, commonly known as vitamin C (overviewed in (Planchon et al., 2004)). Analysis of vitamin C content of apple indicates both genes and the environment factor into vitamin levels, with older cultivars tending to have much higher levels on average than newer varieties (Planchon et al., 2004).

2.2 Approaches to cultivar development

Given the great diversity of apple cultivars as a group and the presence of genetically compatible wild relatives, there are abundant genetic resources available for potentially obtaining apples with desired genetically encoded traits. Apple germplasm collections in countries around the world are valuable resources for conserving and documenting this diversity (Supplementary Table S1). Phenotype screening of collections of wild and domestic apple have identified resistance to fire blight, apple scab, and other diseases, and some individuals even exhibit multiple resistance (Luby et al., 2002; Volk et al., 2008). An addition, extensive research identifying candidate genes or quantitative trait loci (QTLs) for fire blight and apple scab resistance now makes it possible to perform marker assisted seeding selection (MASS) in apple (Ru et al., 2015). Thus, trees and progeny can now be genotyped to track traits genetically. The long juvenile period and lack of self-compatibility of apples in general means is time-consuming to integrate traits and develop cultivars using naturally occurring plant maturation (Pereira-Lorenzo et al., 2018). This approach works well, and breeding efforts started in the 1940s have successfully bred in resistance to apple scab from wild *M. floribunda* into domestic apple (Crosby et al., 1992). Similar efforts to create additional scab-resistant apple cultivars have yielded numerous new varieties, but overall the market success of scab resistant cultivars developed to date has been low (Gessler et al., 2006).

Genetic engineering represents a second and faster option for changing domestic apple. Transformation of domestic cultivars occurred in the 1980s and wild apple is a more recent development (James et al., 1989; Zhang et al., 2021). A variety of genetic engineering approaches have been used in apple, including cisgenesis, transgenesis, RNA interference (RNAi), Viral Induced Gene Silencing (VIGS), and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR, see Table 1 and citations therein). The same apple scab resistance gene introgressed by traditional breeding with *M. floribunda* into domestic apple was transformed directly into Gala apples, maintaining the cultivar background and obtaining resistance in this single generation (Belfanti et al., 2004). Resistance to both apple scab and fire blight occurred with transfer of the *Zea maize* (corn) *Leaf colour* (*Lc*) gene, but the positive gravitropism of the branches meant the trees would be commercially unsuitable for fruit production (Flachowsky et al., 2010a).

Given the long juvenile period of apple trees, one goal of genetic engineering was to produce precocious flowering, which could then be used to shorten generation times and obtain accelerated breeding. This approach required some optimization, as it was challenging to obtain trees that flowered, but not too early. Transgenic addition of *LEAFY* (*LFY*) from *Arabidopsis thaliana* (*Arabidopsis*) led to a more compact and columnar tree form, but no early flowering (Flachowsky et al., 2010b). Overexpression of one *FLOWERING LOCUS T* homolog from domestic apple (*MdFT1*) led to very early flowering with blooms observed while trees were still undergoing *in vitro* cultivation (Trankner et al., 2010). Use of *BpMADS4* from *Betula pendula Roth.* (silver birch) led to the creation of several events, one of which was used to rapidly breed fire blight resistance from an ornamental cultivar of apple to a fruit-bearing cultivar, with five generations occurring in just 7 years (Flachowsky et al., 2007; Schlatholter et al., 2018). This same *BpMADS4* event was also used for introgression of resistance to blue mold from wild *M. sieversii* to

TABLE 1 Examples of apple traits obtained by genetic engineering. Unless indicated, cultivars are domestic apple.

Cultivar(s)	Trait(s) obtained	Target Gene(s)	Method used	Citation(s)
Royal Gala	Firmer fruit	*MdACS*	RNAi	Hrazdina et al. (2003)
Granny Smith Golden Delicious	Non-browning fruits	*MdPPO*	RNAi	Waltz, (2015)
Galaxy	Anthers converted to petals Reduced pollen and seed formation	*MdMADS15 MdMADS221*	RNAi	Klocko et al. (2016)
Gala	Albino plantlets Early flowering	*MdPDS* *MdTFL1*.1	CRISPR	Charrier et al. (2019)
Golden Delicious Gala	Improved resistance to fire blight	*MdDIPM4*	CRISPR	Pompili et al. (2020)
Fuji Ralls Janet Gala	Improved resistance to *B. dothidea* growth on apple callus	*MdCNGC2*	CRISPR	Zhou et al. (2020)
Malus sieverii (wild apple)	Albino plantlets	*MsPDS*	CRISPR	Zhang et al. (2021)
Fuji	Improved resistance to *B. dothidea* fruit rot	*MdCNGC2*	VIGS	Zhou et al. (2020)
Pinova	Columnar tree form	*LEAFY* from *Arabidopsis thaliana*	Transgenesis	Flachowsky et al. (2010a)
Pinova	Early flowering	*MdFT*	Transgenesis	Trankner et al. (2010)
Pinova	Early flowering	*BpMADS4* from *Betula pendula Roth.* (silver birch)	Transgenesis	Flachowsky et al. (2007)
Holsteiner Cox	Increased resistance to fire blight and apple scab	*Leaf colour (Lc)* from *Zea maize*	Transgenesis	Flachowsky et al. (2010b)
Gala	Improved resistance to apple scab	*HcrVF2* from wild apple *Malus floribunda*	Transgenesis	Belfanti et al. (2004)
Gala Galaxy	Improved resistance to fire blight	*FB_MR5* from wild apple *Malus* × *robusta 5*	Cisgenesis	Kost et al. (2015)
Royal Gala	Yellow fruit	*MdPSY1*	Overexpression	Ampomah-Dwamena et al. (2022)
Holsteiner Cox Gala	Increased phenolics in leaves	*MdMYB10*	Overexpression	Rihani et al. (2017)

Gala (Luo et al., 2020). Individuals with or without the *BpMADS4* gene can be identified by DNA testing, allowing for genotyping in each generation (Luo et al., 2020).

In general, genetic engineering approaches are most straightforward with single genes of large influence, but it is possible to target multiple genes at once in apple with RNAi or CRISPR (Klocko et al., 2016; Jacobson et al., 2023). Unlike their conventionally bred counterparts, engineered trees are subject to many regulations, and are challenging to bring to the commercial market.

2.3 Regulatory considerations

Apples and apple products are globally produced and traded, with apples grown in over 90 countries (Nations, 2025). Nearly all apples are conventional crops, produced without genetic engineering, but there is potential for engineered apples to become more prevalent. Currently, non-browning apples obtained by RNAi are grown in Canada and the United States (Waltz, 2015; Duford, 2024). One challenge to wider usage of engineered apples is that regulations regarding definitions and guidelines for genetically engineered crops and crop products are still under development and vary greatly by country and region. Some countries, such as the United States, have guidelines but until recently had no labeling requirements for GMO crops and products. Starting in mid-2025, the United States will now require labeling of foods with ingredients produced by recombinant DNA technology, including Arctic™ apple (Becker, 2023). By contrast, Europe has implemented labeling and monitoring of GMOs, which also included gene-edited crops (Ruffell, 2018). However, a recent decision by the Council of the European Union updated the guidelines to better encompass current plant breeding and modification techniques, which opens up the possibility for future new crop adoptions (Union, 2025). How apple trees such as the fire-blight resistant individuals with the resistance gene introgressed from compatible relatives via genetically accelerated breeding, but which lack transgenes, would be regulated remains to be seen. It is possible that consumers may be in favor of trees produced with these new technologies. There is growing interest in food produced fewer pesticides or fungicides, and if apples produced by new technologies meet consumer needs and desires then regulations may adapt to meet market demand (Rahman et al., 2021).

As science moves quickly, some recent innovations in plant gene targeting offer potential options for achieving transgene-free genome-edited apple trees. It is now possible perform transient CRISPR editing in apple, or to use excision to remove transgenes after edits (Malnoy et al.,

2016; Osakabe et al., 2018; Dalla Costa et al., 2020). These approaches, while not highly efficient, are likely to be faster than using breeding to separate transgenes from edits and would allow for maintaining the overall genetic background of the cultivar used. It is possible that if the targeted changes are small and the transgenes are not stably integrated, apple trees produced with this approach could get approval in the European Union or elsewhere. As the field of biotech crops continues to develop, both in terms of science and regulations, it will be interesting to see what is possible, and which possibilities reach consumers. Both growers and consumers may also be a significant influence in the marketability of engineered apples. Transgenic virus-resistant *Carica papaya* (papaya) trees were created and are credited with saving the Hawaiian papaya industry, which at the time was mostly small farmers (Gonsalves, 2006). More recently, the engineered "PinkGlow" *Ananas comosus* (pineapple) was released in the United States as a novelty item and is popular with consumers (Jay, 2024). Perhaps as more engineered fruits enter the global market apples could be part of the portfolio.

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EDITED BY
Monica Garcia-Alonso,
Estel Consult Ltd., United Kingdom

REVIEWED BY
Drew Lloyd Kershen,
University of Oklahoma, United States
Gabriela Levitus,
ArgenBio, Argentina

*CORRESPONDENCE
Dalia M. Lewi,
lewi.daliamarcela@inta.gob.ar

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Experiences, learnings and perspectives in the regulation of agricultural biotechnology: the view from Argentina

Dalia M. Lewi[1]*, Perla Godoy[2] and Facundo Simeone[3]

[1]Dirección Nacional de Vinculación Tecnológica, Instituto Nacional de Tecnología Agropecuaria, Buenos Aires, Argentina, [2]Coordinación de Innovación y Biotecnología, Secretaría de Agricultura, Ganadería y Pesca, Buenos Aires, Argentina, [3]Dirección Nacional de Bioeconomía, Secretaría de Agricultura, Ganadería y Pesca, Buenos Aires, Argentina

Argentina has established itself as global leader in setting enabling regulations for agricultural biotechnology. Between 2020 and 2023 the responsible administration strengthened this position through the adoption of innovative regulations for New Breeding Techniques and fostering broad international collaboration. The experience accumulated during this period serves to illustrate best practices, current shortcomings, anticipate future challenges, and point to the solutions that the sector will need in the next few years.

KEYWORDS

agricultural biotechnology, regulatory diplomacy, biosafety, regulation, biodevelopment

Introduction

Modern agricultural biotechnology is the technological application of genetic engineering tools to improve crops, microorganisms, and livestock. Its primary objective is to provide benefits to farmers, consumers, industry, human and animal health, and the environment. This technology aims to increase agricultural production, reduce production costs, make more efficient use of resources, promote resilience to climate change while preserving agro-ecosystems, and increase the safety and quality of food.

In 1991, stakeholders within the agricultural sector approached the Argentine government expressing their interest in conducting experimental activities involving genetically modified (GM) plants and seeds. In response, the administration promptly created the National Advisory Commission on Agricultural Biotechnology (CONABIA for its acronym in Spanish). At the time, Argentina already employed professionals with a comprehensive scientific and technical background in modern agricultural biotechnology and was well equipped to fulfil this task. This capacity was recognised recognized by the Food and Agriculture Organization of the United Nations (FAO) in 2014, when CONABIA was nominated as the centre of reference for agricultural biosafety, a recognition still held to date[1]. CONABIA advises decision-makers on the authorization of activities related to genetically modified organisms (GMOs) for agricultural use, whether animals, plants or microorganisms, both for experimental activities and for the commercialization thereof.

1 https://www.argentina.gob.ar/sites/default/files/2022/07/nota_verbal_fao_sobre_conabia.pdf

TABLE 1 Guiding principles for Biotechnology public policy proposals.

i)	Support local bio-developments in biotechnology, bio-inputs, biomaterials, and bioenergy
ii)	sustain and improve the regulatory system, improve regulations and adapt them to local bio-developments
iii)	promote developments with added value at the source
iv)	contribute to the development of the bioeconomy and its application to the country's agriculture, based on the development of bio-inputs and biomaterials, biotechnology, and bio-energies, especially local developments
v)	promote the incorporation of new technologies to improve productivity, with sustainability, paying attention to environmental care
vi)	encourage innovation and development of different crops, centred on regional economies

CONABIA professionals are highly qualified and keep up with the latest scientific advances on modern biotechnology techniques, as demonstrated by the pioneering work performed on the regulation of new breeding techniques, where Argentina was the first country to establish a framework for the assessment of these products.

Actions and public policy proposals

Over the years, different Argentine administrations have been adding depth and innovation to regulatory management, in line with the latest scientific advances. In 2020, the National Directorate of Bioeconomy, which encompassed both the Biotechnology sector and CONABIA, proposed six guiding principles to develop actions and public policy proposals (see Table 1). The proposed principles were not only focused on generating capacities to strengthen regulatory areas. They also focused on facilitating innovation, promoting local research that applied science and technology to develop value-added products for the country. Unlike other countries, where regulatory systems for emerging technologies-such as gene editing-are not yet established or still require substantial capacity building to address regulatory challenges Argentina addressed these challenges over a decade ago. This was made possible by investing in highly trained scientific and technical work force.

One of the fundamental aspects to support local biotechnology research was based on addressing the needs of domestic research groups (Lewi and Vicién, 2020). Concrete actions were implemented to support this, for example, the introduction of the biosafety greenhouses policy for local research. The guidelines for activities including regulated materials (GMOs) had been historically designed for companies requesting the import of seeds to carry out regulated trials in the country. But for local entities developing plant biotechnology, there were some aspects that required further clarity. One of these was the management of genetically modified (GM) plant material generated in laboratories, which had to be transferred to greenhouses under biosafety conditions. These transfers are carried out gradually, with plants grown *in vitro* requiring acclimatization in pots, first in growth chambers and then in greenhouses. The regulation at that time, which required about 6 months between the start of the application and obtaining an authorization, was not feasible. For this reason, a specific regulation was introduced to enable the transfer of plants developed in the laboratory to adjacent greenhouses.

Another policy action was introduced to address uncertainty regarding the regulatory pathway for newly developed local products. In this case, the Ministry of Agriculture provided a consultation window ("Does my product need to be regulated?") in their website. The consultation comprises a series of questions for researchers that are then answered by the technical teams in the Innovation and Biotechnology Coordination, usually within a week. The answers offer advice on whether the product must be regulated by the current regulations, which regulations it should comply with and offering, if applicable, the possibility of a virtual meeting to delve deeper into any technical aspect[2].

As discussed previously, supporting local research in biotechnology was a central focus for the 2020–2023 Argentine administration. As a result, local research in this sector (including plants, microorganisms, and animals), multiplied. To ensure consistent capacity building on biosafety guidelines and ensure compliance with regulations, the administration organised both virtual and in-person trainings (as far as pandemic restrictions allowed), to facilitate understanding and awareness of the regulatory framework and also providing specific consultations for research groups in public and private entities.

Another action was the improvement of the regulatory system and the promotion of new technologies. There is a greater need for new tools and ways of working that help both governments and regulators to better adapt to a changing world and to use regulation as an effective tool to stimulate and direct innovation (Armstrong et al., 2019).

Science is advancing at a rapid pace, and so far, regulation in Argentina has been keeping up with scientific and technological advances. This is in line with the "anticipatory approach" described by Armstrong et al. (2019), which emphasises flexibility, collaboration and innovation. In Argentina regulatory frameworks for different activities are continuously updated, improved, and strengthened, keeping pace with scientific innovations. In the context of GM plants: Argentina updated the evaluation of contained and confined activities and the environmental risk assessment guidelines (ERA), as both are requirements for commercial authorization (see Supplementary Material). These updates strengthened the procedures for evaluation and now include key concepts and methodologies in risk assessment, such as "problem formulation", i.e., values to be

2 Link to the consultation site: https://www.magyp.gob.ar/conabia/

protected, risk hypotheses, pathway to harm (García-Alonso, 2013), and data transportability (Vesprini et al., 2020; García Alonso et al., 2014). These guidelines allow fit-for-purpose risk assessments, considering that the breeding process mitigates unintended effects (Schnell et al., 2015), and avoid information redundancy by applying the concepts of familiarity and history of safe use (Capalbo et al., 2020).

In recent years, a wide variety of advances in biotechnology, molecular biology, and genome sequencing have emerged, these are commonly known by their English acronym, NBT (New Breeding Techniques). One of the best-known technologies within this group is "gene editing", which allows a targeted and specific intervention in the genome.

In 2015, Argentina officially introduced the first NBT normative, applied only to plants. This resolution was the first in the world, providing specific guidelines for the potential regulatory pathways of products derived from new breeding techniques (NBTs), including gene editing. Years later, in 2019, specific normative for animals and microorganisms were also published, and the plant normative was updated.

As a result, Argentina has been a reference point for other countries in the region such as Chile, Brazil, Colombia, Paraguay, Honduras, Guatemala, and Uruguay, all of which have developed their own normative with similar viewpoints, consolidating the adoption of the same criteria in a large part of Latin America. Argentina has since actively participated in international forums and provided training to other countries.

After the experience gained in analysing applications for products derived from NBTs, in 2020 a unification, update, and simplification of the resolution for products derived from NBTs was performed, becoming official in 2021 (Resolution 21/21)[3].

Argentine regulations are based on the definition of GMO used in the Cartagena Protocol, as "an organism that has been obtained through the application of modern biotechnology and that contains a new combination of genetic material." In turn, the definition of "new combination of genetic material" is equivalent to that of "transgenic event" in Argentine regulations: "stable and joint insertion of one or more genes or sequences that are part of a defined genetic construct." These definitions are accompanied by criteria that consider whether that product or improvement could have been obtained through conventional genetic improvement or could have been found in nature.

Cases are submitted individually for analysis at CONABIA through a Preliminary Consultation Instance (PCI). Consultations can include products that are still in the design stage or products already developed and in the commercialisation pathway.

In their response CONABIA confirms whether the product is a GMO or not. For products in the design stage, the response is drafted using the potential tense mode (i.e., the response concludes whether it would be a GMO) and the entities must re-consult when the product has been effectively obtained.

Since this system was implemented, an increased number of requests have been submitted by developers. In fact, an analysis of the PCI cases received showed that: (a) developers were better equipped to predict the costs and estimate the time for product development, even at the design stage. (b) NBT products that are not considered GMOs can enter the market faster than GMO products; (c) a greater variety of traits was introduced in different crop species, animals, and microorganisms, compared to GMO cases; (d) the dynamics and speed of innovation of products obtained by NBT is greater compared to GMOs (Whelan et al., 2020; Goberna et al., 2022).

Regulatory diplomacy

Regulatory diplomacy is about forming and mobilising international networks that allow cooperation with other regulatory agencies worldwide (Warner and Pink, 2023). Argentina has actively engaged in regulatory diplomacy in the field of biotechnology which have provided opportunities for collaborative experimentation, iterative learning, and continuous improvement. Some examples of the main activities undertaken by the National Directorate of Bioeconomy between 2020 and 2023 are provided below.

The "Memorandum of Understanding between the Ministry of Economy of the Argentine Republic and the Ministry of Science, Technology and Innovation of the Federative Republic of Brazil for Cooperation on Biosafety of Modern Biotechnology Products"[4] is an emblematic example of regulatory diplomacy, cooperation, and good practices. Regulators and decision-makers from both countries had been engaging for some time in informal discussions on regulatory oversight within the framework of the Biotechnology Commission of the SGT8 ″Agriculture" of MERCOSUR and the Working Group "Policies for Biotechnology" of the Southern Agricultural Council. But it was not until the end of 2020 and during 2021 that these discussions turned into concrete actions for defining common criteria and objective regarding agricultural biotechnology. The memorandum provides a framework for collaboration between the regulatory agencies of both countries, streamlining and facilitating the evaluation and approval of biotechnological products within the agricultural sector. The main objectives of the agreement are listed in Table 2.

Under this agreement both countries conduct the joint evaluation of applications for authorization of biotechnological products. This introduces important efficiencies such as streamlining processes, reducing costs and facilitating synchronous approvals, which in turn facilitate bilateral trade. The key benefits of the agreement are: greater competitiveness, enabling developers from both countries to develop and commercialize biotechnological products more efficiently, increasing their competitiveness in the global market; sustainable development: the agreement contributes to the adoption of technologies that allow for increasing food production in a

3 https://magyp.gob.ar/sitio/areas/biotecnologia/conabia/_pdf/Resolution_N21-2021_3%20annexes.pdf

4 https://www.magyp.gob.ar/internacionales/mous-brasil.php

TABLE 2 Main objectives of MOU Argentina- Brazil.

No	Objective	Refers to
1	to reduce costs and time	simplify regulatory processes for developers of biotechnological products, especially for small and medium-sized enterprises
2	to promote local and regional innovation	promote the development of new technologies in the agricultural sector, such as gene editing and biotechnology
3	to strengthen bilateral trade	facilitate the exchange of biotechnological products between both countries, avoiding unnecessary regulatory barriers and especially asynchronies in the authorization of products that potentially lead to disruptions in trade
4	to guarantee food safety	ensure that biotechnological products are safe for human and animal consumption, and that they do not have negative impacts on the environment

sustainable manner, reducing environmental impact; and strengthening the bilateral relationship: cooperation in the field of biotechnology deepening commercial and scientific ties between Argentina and Brazil. In summary, this agreement represents an important step towards the integration of the regulatory systems of both countries in the field of biotechnology, which fosters innovation, facilitates trade, and increases sustainable development in the region.

Argentina, Brazil, Paraguay, and Uruguay have taken a significant step towards working together in the development of science and technology applied to food production, with the creation of the International Network for Biosafety of Modern Biotechnology Products (ABRE-BIO). The network comprises institutions from each of the four countries that control and guarantee the biosafety of Genetically Modified Organisms (GMOs), gene editing and New Breeding Techniques (NBTs). In this context, biotechnology is viewed as a key element in modern agriculture, not only to meet the priority objective of producing healthier food, and in a more sustainable manner, as the world demands, but also to enable the generation of employment, development, and wellbeing in the rural areas of the countries involved.

The network was formalized through a multilateral memorandum of understanding signed on 23 August 2023, at the end of the Southern Agricultural Council (CAS) meeting and, formalized in June 2024. It is expected that more countries will join in the near future. It is expected that this network will allow for closer cooperation in innovation in the agricultural, agro-industrial, and agri-food sectors by four countries that make a key contribution to sustaining global food security. It will also promote the exchange of professionals and scientific information related to biosafety and risk assessment of GMOs and the technical evaluation of products derived from NBTs. It will also lead to reduction in cost and time in regulatory oversight. Additionally, it will provide opportunities for further harmonization. The countries in this network are also aligned in the aim of fostering local bio-developments, both public and private. This represents an example of deepening commercial relations, that do not compromise on safety and promote sustainable production systems and food security.

Argentina, through the National Directorate of Bioeconomy (DNB), promoted the creation of the Global South Bioinnovation Group (BIGSUR), a group of global countries in southern regions (Latin America, Africa, and Southeast Asia) that encourages the creation of an enabling environment for scientific research and innovation aimed at accelerating local solutions to food security, climate change, and biodiversity loss through active cooperation and joint actions.

BIGSUR held its first meeting on May 18 and 19, 2023, at the Secretariat of Agriculture, Livestock and Fisheries (SAGyP) in Buenos Aires, Argentina. The meeting was attended by regulatory representatives from 13 countries (Argentina, Brazil, Chile, Uruguay, Peru, Paraguay, Costa Rica, Colombia, Honduras, Nicaragua, Kenya, Nigeria, and Ghana), to discuss topics relating to agricultural biotechnology and gene editing and explore common positions regarding regulation and innovation. A second meeting co-organised by Argentina and Kenya took place August 23, 24, and 25 of the same year in Nairobi, Kenya. This time the meeting was attended by regulatory representatives from 19 countries (Argentina, Brazil, Uruguay, Paraguay, Colombia, Honduras, Kenya, Nigeria, Ghana, Burkina Faso, Ethiopia, Malawi, Mozambique, Rwanda, Zambia, Zimbabwe, Tanzania, Philippines, and Bangladesh).

The event aimed at consolidating the group of southern countries, creating a forum for harmonizing and coordinating regulations on innovative biotechnologies (such as gene editing), to share experiences and knowledge, and to align common messages to share in multilateral forums.

Within the framework of the event, the Argentine delegation from the DNB provided training to countries in the analysis of hypothetical cases of gene editing products, with the intention of enabling regulators and decision-makers in the countries to make science-based decisions to promote local developments and new biotechnological solutions to food security and climate change. The event aimed to improve participants' understanding of how the regulatory approach affects the adoption of innovative technologies.

It is considered that genome editing techniques can add value to existing agricultural practices in a way that improves sustainability while respecting biodiversity and addressing climate change. Ongoing research with CRISPR/Cas9 and other techniques in Latin America, Africa, and Southeast Asia show great potential to contribute to the accelerated achievement of the Sustainable Development Goals (SDG).

Countries of the Latin America and the Caribbean (LAC) region, Africa, and Southeast Asia are currently at different stages of development of their regulatory frameworks for biotechnology. Understanding these complex and dynamic interactions is key for developing governance and investment strategies that are appropriate and acceptable for each region.

The Southern Agricultural Council (CAS) is another example of a regulatory forum that fosters dialogue, consultation, and coordination of actions at the ministerial and regional level on matters concerning the sustainable development of the agricultural,

forestry, and fisheries sectors, animal and plant health, food safety, as well as international negotiations on trade in agricultural, fisheries, and forestry products. Composed of the Ministers of Agriculture, or their equivalents, of Argentina, Bolivia, Brazil, Chile, Paraguay, and Uruguay, it was established in 2003 through the signing of an agreement and ratified in 2005 on the VII Ordinary Meeting of the CAS. It is chaired by the Ministers of Agriculture of the member countries. The CAS has a network of regional technical groups that support and implement ministerial decisions. These specialized groups make up the Agricultural Policy Development Network (REDPA) and take part in different projects and actions according to the needs and priorities of the region. Its primary function is to define the topics and priorities of the regional agricultural and forestry agenda, as well as to articulate the development of the agreed actions.

As a sectoral forum for the analysis of the problems of sustainable development of the sector, CAS focuses particularly on evaluating development policies and programs, the progress of trade negotiations, and agreeing on positions for participation in multilateral, plurilateral, and bilateral forums with countries or blocs outside the region. Evaluating the sanitary and phytosanitary situation of the region and coordinating control and eradication actions for sanitary and phytosanitary problems, as well as coordinating positions in relation to the work carried out in international standardization forums are also leading activities of this forum. Working Group 5 (WG5) of the CAS - Public Policies on Biotechnology Working Group No. 5, called Public Policies on Biotechnology, meets regularly every year and has two declarations at the World Trade Organization (WTO) supporting new biotechnologies and best regulatory practices. In addition, in May 2023 WG5 published a document on biotechnology in the region aimed at providing information about the benefits of using biotechnology and its potential as a tool for agricultural production, biosafety in the environment, and food safety for both humans and animals[5].

There are other instances where Argentina exercises regulatory diplomacy in negotiation forums for issues relevant to biotechnology and agriculture: the Convention on Biological Diversity, the Cartagena Protocol, the Organisation for Economic Co-operation and Development (OECD), etc., and other events where regulators from Argentina and BIGSUR countries meet to discuss and coordinate activities: such as the International Symposium of Biosafety Research, the Seed Association of the Americas Congress, Like Minded Group meetings, etc. These participations are essential to collaborate in the formulation of international agreements and regulations that directly impact the agricultural sector, as well as to prevent the advancement of binding issues that could affect the way biotechnology is produced and applied in the sector. It is also important to participate in events where the objective is to promote scientifically sound research that supports the evaluation of biosafety by improving communication between scientists who study plants, animals, and microorganisms with new characteristics produced through modern biotechnology. In summary, it is important to have a group of countries with similar ideas and common spaces where regulatory diplomacy can be exercised, a field that is closely linked to the intellectual and regulatory "battle" over agricultural technologies. These activities should be carried out always recognizing that agricultural production will need to be substantially increased to meet global food demand, understanding that innovative agricultural technologies must continue to play a critical role in addressing these challenges, and emphasizing that regulatory approaches must have a scientific basis.

Capacity building is another example where Argentina has been exercising regulatory diplomacy. Since 2014, Argentina has been recognized as a Reference Centre for Biosafety of Genetically Modified Organisms (GMOs) by FAO. This recognition has facilitated the country's engagement with more than 20 countries[6] strengthening their regulatory capacities and providing technical assistance with topics relating to the biosafety of modern biotechnology (Table 3). In 2023, the Agreement with FAO was renewed for the third time until2027[7].

With more than 30 years of experience in the evaluation, regulation, and promotion of agricultural biotechnology, and with the goal of facilitating technology transfer and bilateral trade between countries, Argentina has been one of the first countries to develop and apply biotechnology techniques to promote the development of primary production. These achievements also reflect FAO recommendations regarding their importance in improving food production, reducing production costs, benefiting the environment, and promoting developments that, in line with scientific advancements, allow to produce ever-increasing quantities of safe, harmless, and high-quality food.

In this regard, Argentina has collaborated with more than 20 countries, strengthening capacities and providing technical assistance on biosafety of modern biotechnology (Table 3).

The experience gained in Argentina demonstrates that, although there is heterogeneity in the progress and maturity of regulatory systems across countries, positions can be brought to closer alignment and a common regulatory language can be found, promoting the use of shared criteria. This was demonstrated by the discussions that took place during the BIGSUR workshops. Even when different countries were at different stages in their regulatory journey, the examples discussed revealed a number of similarities in criteria and conclusions. The application of sound scientific criteria and harmonized definitions facilitate this task. This was particularly evident at a workshop in Kenya in August 2023 where regulators from different countries met to analyse and discuss case studies of products derived from gene editing. Once the conclusions from these case studies were shared, it became clear that the criteria that the different countries had

5 http://consejocas.org/wp-content/uploads/2023/07/Publicaci%C3%B3n-Evoluci%C3%B3n-del-uso-de-la-biotecnolog%C3%ADa-en-los-pa%C3%ADses-del-CAS.pdf

6 https://www.magyp.gob.ar/internacionales/pdf/Catalogo-de-Proyectos-FOAR-Area-Biotecnologia.pdf

7 https://www.argentina.gob.ar/sites/default/files/2022/07/ae_04–2023_4_1.pdf

TABLE 3 Capacity building activities in the recent years.

Year	Country
2020/2023	Perú: project "Strengthening Capacities for Activities with New Breeding Techniques (NBT), including Gene Editing", founding by the Argentine Fund for South-South and Triangular Cooperation "FO-AR"; Two missions in 2022 (Buenos Aires-Lima) and three missions in 2023 (Lima-Buenos Aires-Lima)
2019–2021	Cuba: Workshops for training Cuban technicians and officials in biotechnology and biosafety within the framework of the "FOAR Cooperation Project between Argentina and Cuba"
2020	Panama: Training course for Panamanian officials within the framework of a United Nations GEF Project, "Strengthening National Capacities for the Full Implementation of the Cartagena Protocol on Biosafety in Panama," and with CONABIA as a global reference center for biotechnology training. November 2020
2021	Thailand: Webinar: Exchange of experiences in Agricultural Biotechnology in Argentina and Thailand. December 2021
2022	Egypt: Virtual training for officials and regulators from the Agricultural Research Center of Egypt, as part of a training requested by Egypt and organized by the Argentine Embassy in Egypt. Seminar on Modern Biotechnology for Agriculture and Agroindustry - Training provided to professionals from Egypt

applied were similar and the conclusions reached were also similar. This exercise shows that, although countries may have different regulations or are at different stages of implementation, the application of scientific criteria and reasoning based on similar globally adopted definitions are fundamental. Another observation was that differences in terminology to the same processes and/or products in gene editing applied in different countries pose a challenge. To address this, the delegates agreed to adopt common terminology that would facilitate the differentiation between GMO products and gene edited products. Some of the definitions discussed related to the terminology associated with GMOs and NBTs. The proposal was that GMOs should be referred to as "GM" or "biotechnological or transgenic crops", while those derived from NBTs -that are not considered GMOs-should be referred to as "non-GM" or "new product" or "variant". Regarding the method used to develop the products, the proposal is to describe the methods to produce a GMO as genetic modification or transgenesis and for NBT products as "genetic intervention". The steps leading to the commercial approval of these products are also different, while for GMOs, a pre-market risk assessment is conducted, for NBT products a technical evaluation is carried out to determine the regulatory status that leads to a conclusion or technical opinion. It is also important to emphasize that all products are regulated until they obtain their commercial authorization. In Argentina all crops require a variety registration that is overseen by National Seed Institute (INASE).

Regulatory challenges (what lies ahead)

Until the publication of this review, Argentina's NBT normative has been sufficient to resolve the regulatory status of the cases presented. Most of these cases referred to specific gene editing involving single base replacements or deletions of sections of a gene sequence to silence its expression. However, the advancement of scientific developments and the application of new technologies are leading the analysis towards more complex cases that could potentially challenge this normative.

Regulatory anticipation can maximize opportunities and mitigate the potential risks associated with emerging technologies (Armstrong, 2019). Anticipated applications of gene editing tools in the near future include multiple gene edits, gene duplication, allelic replacement, chromosomal rearrangements (inversions, translocations), polyploidization, and the utilization of gene editing to generate variability for genetic improvement.

In the broader context of agricultural biotechnology, the following challenges include: alternative protein production; cell-cultured food; molecular farming (production of molecules in alternative matrices); genetically engineered bio-inputs for agriculture and products impacting human and animal health, such as organs for xenotransplantation from genetically modified (GM) or gene-edited animals, GM insect vectors for disease transmission prevention, and GM insects for pest control. In this sense, international harmonization and cooperation would be crucial for addressing these challenges.

Conclusion

The development of agricultural biotechnology and its regulatory framework has become a state policy in Argentina. Strengthening the institutional capacities for the regulatory oversight of biotechnology derived products has enabled the development of regulations based on scientific and technological advances. Notably, between 2020 and 2023 there was a special focus on providing support for innovation and development of local research.

These advances were enabled by building a highly qualified workforce with strong scientific backgrounds encouraged to follow the latest scientific developments and engaged with the international regulatory and scientific community.

While international forums propose to discuss and address regulatory harmonization, each country should develop its own regulations, considering its own sovereignty based on the values to be protected established in its constitutional principles, laws, and regulations. However, bilateral, regional, and multilateral dialogues are conducive to encourage the use of a common regulatory language and terminology, in which the definitions of the products subject to regulation and analysis are clear and agreed upon.

Successful international regulatory cooperation hinges on two critical conditions: fostering trust and facilitating knowledge

exchange among regulatory bodies. These elements promote constructive dialogue, collaborative evaluation sharing, and the establishment of a trusted environment for discussing current and emerging challenges, particularly those posed by novel technologies. Such knowledge sharing streamlines communication and facilitates consensus building while respecting the sovereign decisions and perspectives of each nation. These dialogues should prioritize the wellbeing of stakeholders engaged in the scientific and technological advancement of each community, focusing on addressing specific local challenges. This approach stimulates interest in problem-solving, identifies necessary resources, and defines regulatory requirements for case-by-case assessments of agro-environmental biosafety and food suitability.

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EDITED BY
Lijun Shang,
London Metropolitan University,
United Kingdom

REVIEWED BY
Yang Xue,
Tianjin University, China
Maria J. Espona,
Caucasus International University, Georgia

*CORRESPONDENCE
Carmen Vicien,
cvicien@gmail.com

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Genetically modified microorganisms for agricultural use: an opportunity for the advancement of risk assessment criteria in Argentina

Clara Rubinstein[1], Gabriela Levitus[2], Carmen Vicien[1,3]*, Natalia Andrea Modena[4], Sandra Ruzal[5], Facundo Vesprini[4], Dalia Marcela Lewi[6], Cecilia Caminoa[7], Maria Fabiana Malacarne[8], Nerina Francescutti[4] and Juan Ignacio Amaturo[9]

[1]Institute for Scientific Cooperation on Health and the Environment (ICCAS), Buenos Aires, Argentina, [2]Argentine Association for the Development and Education in Biotechnology (ArgenBio), Buenos Aires, Argentina, [3]School of Agriculture, University of Buenos Aires, Buenos Aires, Argentina, [4]Bayer Crop Science, Buenos Aires, Argentina, [5]Biochemistry Institute, Exact and Sciences School, University of Buenos Aires, Buenos Aires, Argentina, [6]Instituto Nacional de Tecnología Agropecuaria, Buenos Aires, Argentina, [7]BASF SA, Buenos Aires, Argentina, [8]Argentine Seed Association, Buenos Aires, Argentina, [9]Corteva Agriscience SRL, Buenos Aires, Argentina

The development and use of biologicals in agriculture is of growing interest globally. The potential of these tools to increase and protect yield complementing other tools has stimulated the interest of developers. Agricultural countries like Brazil and Argentina in Latin America have extensive experience with the use of biologicals for biocontrol and as seed inoculants. The last decade has seen the number of bio-based startups grow in the region, many of those dedicated to the development of microbial based bio-inputs. The potential for improving the efficacy and functionality of these products by means of gene technologies is very promising; however, the regulatory oversight of these innovations needs adaptation to become fit for purpose. The Biotechnology Working Group at ICCAS identified the need for a science-based discussion on this matter and considered alternatives to the current paradigm, developed over 30 years ago for transgenic plants.

KEYWORDS

microorganisms, bio-inputs, biologicals, risk assessment, biosafety

Introduction

The Institute for Scientific Cooperation on Health and the Environment[1] (ICCAS in Spanish) is a scientific non-for-profit association based in Argentina, which brings together experts from academia, industry and government and provides a neutral forum to discuss scientific matters of public interest. The Biotechnology Working Group has over 25 years of existence driving numerous capacity building programs in the Latin American region,

1 https://iccas.org.ar/en/home

hosting scientific discussions on biosafety criteria and developing conceptual tools for the risk evaluation of products derived from modern biotechnology (Garcia-Alonso et al., 2014; Beker et al., 2016; Fernandez Ríos et al., 2018; Capalbo et al., 2020; Vesprini et al., 2020). This working group identified a need for a scientific discussion to explore science-based approaches adapted to the case of genetically modified microorganisms (GMM) for agricultural use, with focus on bacteria.

Initially, discussions touched on the appropriate safety measures to conduct experimental field trials with GMM under the current biosafety paradigm applied in Argentina, originally developed for GM plants. However, the profoundly different nature of microorganisms as compared with plants - microorganisms are not sessile and the genetic exchange mechanisms between them are completely different and diverse - led to a more general question about how risk assessment criteria should be applied to these cases, even beyond experimental releases. It was clear then, that in order to facilitate the safe deployment of these innovations, an adaptation of the assessment criteria was required to become fit for the purpose of the microbial world. Similar discussions are also taking place in other regions and venues (OECD, 2024b), as biological tools are increasingly becoming part of sustainable agriculture strategies, and the challenges to use the safety assessment criteria created for plants become evident.

The present work reflects the result of these discussions, intends to contribute to a science-based approach adapted to the nature of these products - which are not chemicals nor plants - and bring to light the need for a paradigm shift to assess their biosafety. The aim of this work is to present specific aspects of the biology and genetics of microorganisms (in particular bacteria) that are relevant to risk assessment and management.

Use of microbial based bio-inputs in the region

Different functional groups of microorganisms are applied to agricultural production. Biofertilizers promote growth in plants through nitrogen fixation or phosphorus solubilization mechanisms. Nitrogen-fixing bacteria can be free-living, endophytic, or nodulating (Laranjo et al., 2014; Silva et al., 2023; Kramer et al., 2020). Phytostimulants include phytohormones producers or promoters of plant growth through direct mechanisms. Biocontrol agents, on the other hand, include the so-called microbial biopesticides, which act through the production of larvicidal toxins, bacteriocins, biosurfactants, antibiotics or cell wall-degrading enzymes. Other biocontrol mechanisms involve inhibition of the quorum sensing of the pathogens or the induction of systemic resistance in the host plants (Gómez-Godínez et al., 2023; Legein et al., 2020).

Nitrogen -fixing inoculants make up around half of the global biofertilizer market, while over 55% of the globally marketed biopesticides are microbial (Aramendis et al., 2023); Europe and Latin America are the top users. Over 20 million hectares of soybean are planted every year in Argentina, most of which are treated with over 25 million doses of biofertilizers. In 2022, close to 25 million doses of formulations based on *Azospirillum* sp. were used in Argentina and Brazil for the treatment of corn, soybean, peanuts, common bean, wheat, sorghum, sunflower and horticultural production (Barbosa et al., 2021; Compant et al., 2025).

Argentina has a 40-year history of research, development and agricultural use of bio-inputs and it was one of the first countries to release a commercial product containing an *Azospirillum brasilense* strain back in 1996 (Cassan and Diaz Zorita, 2016). Biocontrol agents have been used in Latin America since the late 19th century and are currently used on a large scale, being the region with the largest historical adoption (Biaggioni et al., 2013; Gottems, 2021).

Latin America is also a hub for innovative startups with Argentina, Brazil, and Chile leading in the biotechnology sector thanks to the large research community and the relevance of agricultural and food chain applications in these countries (Peña and Jenik, 2023).

Microbial formulations are subject to biotic and abiotic factors that affect their performance, stability or consistency in the fields. Both classical and emerging strategies are applied by developers and researchers to address these problems (Batista and Singh, 2021), with gene technologies having great potential, although these will require adaptive risk assessment criteria.

Regulatory context for conventional bio-inputs in Argentina

The National Service for Agri-food Health and Quality (SENASA) is the responsible agency for the registration of these products and has recently issued an updated normative for biological pesticides and fertilizers (SENASA, 2023). Within this framework, experimental releases of conventional microbial bio-inputs are not subject to a regulatory permitting process for proof of concept, selection of candidates or efficacy testing purposes, among others. However, for imported microorganisms, authorizations to introduce samples for testing are needed and the amount requested for each trial needs to be specified. A characterization of the imported microorganism is also required, focused on pathogenicity, toxicology and eco-toxicology. The most frequently requested microorganisms for import are viruses for biocontrol and plant growth promoting bacteria. In all cases, for commercial registration, a complete data package for safety assessment is required.

The case of genetically modified microorganisms (GMM)

Argentina has extensive experience with the risk assessment of biotechnology derived products. CONABIA (the National Advisory Committee for Agricultural Biotechnology) was created in 1991 and was the first of its kind in the Latin American region. Ministerial Resolution 763/2011[2] rules the oversight of GMO and both CONABIA and the Biotechnology Food and Feed Safety Coordination at SENASA are involved in the regulatory

2 https://servicios.infoleg.gob.ar/infolegInternet/anexos/185000-189999/185806/norma.htm

assessment process for commercial authorization (CIB GM crops, 2025).

An environmental risk assessment for GMO is currently implemented, originally developed for GM plants and updated over time. The risk assessments for both contained/confined activities and commercial production are carried out by the technical staff of the Biotechnology and Innovation Coordination at the Agriculture, Livestock and Fisheries Secretariat and by CONABIA[3].

A specific guideline for GMM has been developed following the same model (Resolution 5/2018 and Resolution 52/2019) and is presently being updated to consider the scientific and technological state of the art (CIB GMMs, 2025). So far, several GMM for industrial uses or vaccines have been approved, but no GM bio-inputs have been authorized for experimental or commercial environmental release in Argentina[4].

Genetically modified microorganisms (GMM) and scientific risk assessment criteria

The WG discussions focused on the unique challenges posed by GMM, as the profound differences between microorganisms and higher organisms makes it very difficult to apply the same criteria developed over 30 years ago.

Microbial diversity is a dynamic phenomenon resulting from highly plastic adaptation processes mediated by mutations, exchanges and horizontal gene transfer events. Genetic exchange mechanisms have been well characterized in microorganisms, with conjugation, transduction and transformation being the main ones (Arnold et al., 2022; Magnabosco et al., 2024). Conjugative transfers of broad-host range plasmids and transformation of chromosomal genes occur in different environments, including in planta, also between remotely related microorganisms (Kay et al., 2003). For these reasons, defining species is not trivial for microorganisms and thus it is not appropriate to apply the same logic to interpret phylogenetic relations used for higher organisms (Kunin et al., 2005; OECD, 2003), or to refer to the "compatible species" paradigm to assess potential risks of gene dispersion.

This said, it is important to also consider that there are natural barriers to exogenous DNA (restriction-modification, CRISPR-like and related mechanisms) and that GMM are generally unfit to survive and multiply in nature due to several factors (expression burden, genomic disruption, domestication). Mutations, chromosomal rearrangements and other mechanisms can improve microorganisms for bioproduction purposes but make them generally less fit in the environment, where local microbiota can act as an ecological barrier (Steensels et al., 2019).

The environmental release of GMM is not new. Since the first field trials to evaluate GM *Pseudomonas syringae* ("Ice minus" strain) in the 1980s, GMM have been investigated for decades by both academia and industry (Ke et al., 2021; De Leij et al., 1995; Wilson and Lindow, 1994). Laboratory and field research in experimental plots made it possible to monitor and trace modified bacteria to assess their survival, dispersion and effects on the local microflora. This research showed no relevant differences between the modified bacteria and their parental strains in terms of survival, spread or persistence, and observed effects on resident microflora were transient, or limited and less pronounced than those induced by conventional agronomic practices (Amarger, 2002; Chemla et al., 2025).

Back to the basics: comparative approach, the familiarity concept and the issue with the definitions

> As Dr Hiroshi Yoshikura stated in the context of the OECD workshop held in 2015[5] to discuss this topic: *"One approach could be going back to the two complementary concepts developed by OECD in early 1990s: familiarity and substantial equivalence"* (Yoshikura, 2015). This recommendation seems the most reasonable to enable an evidence-based risk assessment of GMM, as the conceptual framework based on the fundamental pillars developed for Modern Biotechnology can be adapted to the particular biology of microorganisms without compromising the robustness of the biosafety assessment (OECD, 2015). The comparative approach, developed decades ago for biotechnology derived plants (OECD, 1986), was considered and still is the most robust approach to establish the "substantial equivalence" of the new organism compared with a "*conventional counterpart with a history of safe use*" (OECD, 1993b; Codex, 2003), also considering familiarity as proposed back in 1993 as an essential part of the Problem Formulation process (OECD, 1993a; Capalbo et al., 2020).

Another key element to consider is the regulatory definition of a GMM. GMO definitions are not harmonized and different versions or interpretations bring additional complexities (De Schrijver et al., 2024). In fact, depending on the definition, microorganisms improved by classical genetics or techniques resulting in changes that could have been obtained through classical genetics, could end up being categorized as GMM. Gene technologies that may introduce specific regulatory sequences or leave non coding structural traces ("scars") in the genome could end up being subject to the regulatory oversight for GMO if unfit definitions are in place (Chemla et al., 2025).

Historically, it was generally accepted what a GM plant or animal was, until the advent of gene editing disrupted this virtual consensus (Podevin et al., 2012) and this is now further disrupted with the need to re-think what a GM microorganism is. As Lensch et al. (2024) have recently pointed out, "*The terms GMOs and non-*

3 https://www.argentina.gob.ar/agricultura/bioeconomia/biotecnologia/documentos-de-decision-conabia

4 https://www.argentina.gob.ar/microorganismos-gm-con-autorizacion-comercial

5 Hiroshi Yoshikura, National Institute of Infectious Diseases, Ministry of Health, Labour and Welfare, Japan.

GMOs are no longer fit for purpose. Even more clearly than in plants, the boundaries between "genetically modified" and "conventional" microorganisms have become blurred".

The assessment approach discussed in the next section intends to apply the logical processes of Problem Formulation and the Paths to Harm to the risk assessment of GMM, focusing on the equivalence of the GMM with the host microorganisms and considering the degree of familiarity with the hosts, the environment, the trait and the intended uses.

Proposal for the identification of acceptable risks for the environmental release of GMM: a fit for purpose approach

The WG addressed some questions about the evidence needed to evaluate the risks for the environmental release of GMM. Some key considerations were firstly identified to frame the discussion, namely:

- Given the available knowledge of microbial genetics, physiology and metabolism, and the analytical methodologies used in microbiological research (bioinformatics, high throughput DNA sequencing and metagenomics, cultivation-independent community analyses, novel cultivation methods, antimicrobial sensitivity assays, among others), in most cases a complete characterization can be generated under laboratory and/or greenhouse conditions for conventional or GM microorganisms (Janssen et al., 2002; Stevenson et al., 2004)
- Current registration requirements for conventional agricultural bio-inputs cover the majority of relevant biosafety aspects, like toxicity, pathogenicity, antibiotic resistance or production, among others; so, these are not unique to GMM.
- Generally, the main objective of experimental field releases of bio-inputs is to test efficacy.

With these in mind, three main questions were discussed:

- *What information is essential to make a decision about the risk of releasing a GMM?*
  The required information should derive from a sound Problem Formulation and the Paths to Harm exercises (see below).
- *Which biosafety related endpoints would be measured in the field that could not be measured in lab or greenhouse studies?*
  Even when a complete characterization of the host microorganisms as well as the trait incorporated in the GMM can be achieved during the discovery/development/design phases, on a case by case basis and hypotheses driven, some endpoints could require field trials to be measured.
- *When needed, which management measures should be applied to experimental releases of GMM?*
  Measures like limited acreage, buffer zones, distances from commercial crops, etc., can be implemented based on the risk hypotheses identified. The life cycle, the mode of action and the intended use (i.e., vegetative vs. sporulating microorganisms, free living vs. symbiont or endosymbiont, inoculation vs. foliar spraying, etc.) will determine if additional measures such as drift reduction or monitoring might be required, based on plausible risk hypotheses.

Problem formulation and the paths to harm for genetically modified microorganisms (GMM)

The Problem Formulation (PF) process is a well-established methodology for risk assessment currently applied by numerous agencies and risk assessors globally (Garcia-Alonso, 2013).

The process starts by framing the case and defining the scope of the assessment focused on the protection goals that are relevant to the case. The second step involves gathering the available knowledge on the case under review and related cases. In fact, considering what is known (familiar) is extremely important. In the case of GMM, a thorough characterization along with the degree of familiarity with the host microorganisms and the novelty of the expressed traits will guide the assessment.

The central step in PF is the identification of plausible and testable risk hypotheses (defined as scientific hypotheses specifically focused on the risks of adverse effects to the relevant protection goals), based on the information that is already available and the similarity to the non-modified host (comparative approach).

Going back to protection goals, these are not always defined in policies, however, there are general goals that can be a starting point and provide the basis for the process. This said, more refined, operative goals are needed to be able to assess relevant exposure scenarios (Garcia-Alonso and Raybould, 2014).

Some globally established protection goals are human and animal health, agricultural production and ecosystem services. Operative goals are generally related to the protection of beneficial organisms and the preservation of commercially important crops. Having clear protection objectives is key to performing robust, evidence-based risk assessments.

Once relevant operative goals are defined and risk hypotheses identified, the last step is to analyze the possible paths to harm under probable exposure scenarios in order to verify which hypotheses are of possible occurrence and establish a study plan to test them if there is not available data (OECD 2024b; Gray, 2012).

In summary, applying the comparative approach based on PF would provide an adequate evidence base for decision-making and enable the safe deployment of bio-inputs based on GMM. In cases where this process identifies the need for field trials, the data packages generated in lab-greenhouse studies and the familiarity with the host and traits should allow safe experimental releases with reasonable management measures (see Figure 1)

Considering all the above, the general conclusion was that releases for experimental purposes (like efficacy testing) can be allowed with an appropriate risk assessment based on available information. As other trials subject to regulatory oversight, these would require to provide a detailed protocol with evaluation objectives, management of the trial from planting to harvest, etc.

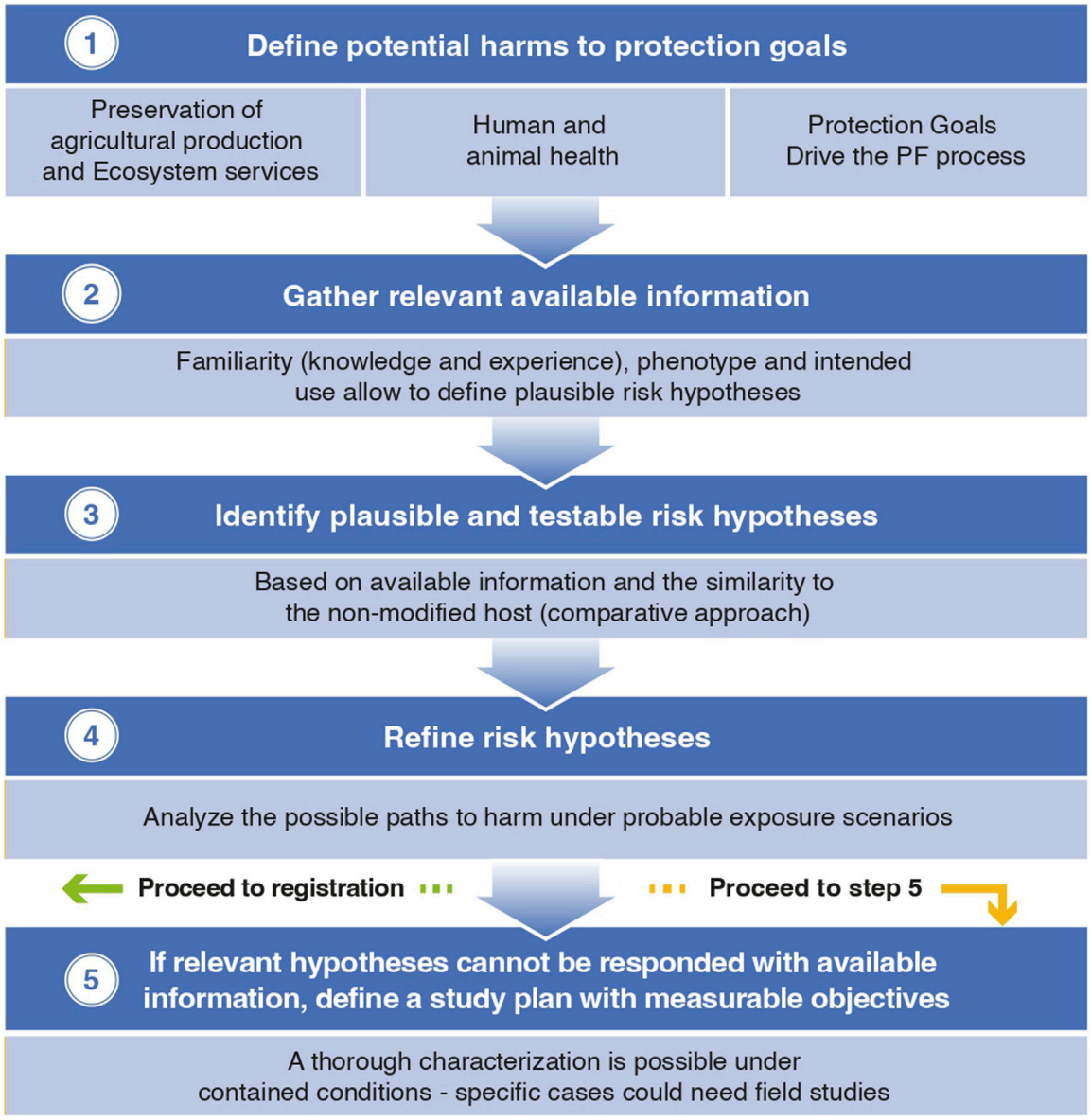

FIGURE 1
Problem Formulation Sequence applicable to GMM.

Upon reporting of the trials results and provided no additional concerns are raised, a final decision on the biosafety of the GMM should be possible. With this, the registration process would proceed as with conventional bio-inputs, which -as above detailed-need to provide a complete safety data package.

Discussion: a paradigm shift is in order

Following a sound PF process for the defined protection goals is the best science-based way to identify potential risks and any missing data that might be needed to release a GMM. In contrast to plants, where field experiments are needed for event selection and characterization, and for which confinement conditions are well defined and managed, a complete dataset for the characterization of microorganisms can be generated in laboratory and greenhouse studies.

If the necessary information identified during PF is available, experimental releases would be possible with basic management measures, as discussed. Once established that the GMM will not introduce new risks to health or the environment, the safety assessment of the bio-inputs based on the GMM could follow that of conventional strains for registration.

As noted, the advent of gene editing tools revealed the need to revisit the risk assessment criteria and the definition of a GMO, and GMM are now renewing this challenge. The GMM status depends on the definitions in use and the current one has been developed with higher organisms in mind. A new definition would need to be developed for microorganisms based on criteria that consider the particular nature of their biology.

When considering biosafety, design strategies are and will be critical to ensure safe releases of GMM. Biocontainment strategies currently available and under development can provide higher levels of biosafety when appropriate: besides genomic insertions-considered good general practice-auxotrophy, transcriptional control, gene entanglement and xenobiology are some examples (Gómez-Tatay and Hernández-Andreu, 2024; Chlebek et al., 2023; Chemla et al., 2025). Also, noteworthy, advanced technologies are transforming the research and development of biologics, combining big data and artificial intelligence to design innovative products, which will require adaptive, fit for purpose criteria (Wang, 2025).

Changing the current paradigm would be an important contribution to the development of innovative bio-inputs, which can be delayed if field testing with GMM is perceived as not possible due to the difficulties to meet requirements, in particular by small companies, public sector or startups (Chemla et al., 2025; Thakor and Charles, 2025). Finally, interdisciplinary work and regulatory pre-consultations, as is implemented in Argentina, are extremely important for both developers and regulators, as these instances inform regulators, allow for guidance to developers and add transparency to the whole process (OECD, 2022; OCED 2024a).

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

CR: Writing – review and editing, Writing – original draft. GL: Writing – original draft, Writing – review and editing. CV: Writing – review and editing, Writing – original draft. NM: Writing – original draft, Writing – review and editing. SR: Writing – original draft, Writing – review and editing. FV: Writing – review and editing, Writing – original draft. DL: Writing – review and editing, Writing – original draft. CC: Writing – review and editing, Writing – original draft. MM: Writing – review and editing, Writing – original draft. NF: Writing – original draft, Writing – review and editing. JA: Writing – original draft, Writing – review and editing.

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Conflict of interest

Authors NM, FV, and NF were employed by the company Bayer Crop Science. Author CC was employed by the company BASF SA. Author FM was employed by Argentine Seed Association. Author JA was employed by Corteva Agriscience SRL.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY
Stuart Smyth,
University of Saskatchewan, Canada

REVIEWED BY
Felix Moronta-Barrios,
International Centre for Genetic Engineering and Biotechnology, Italy

*CORRESPONDENCE
Danilo Fernández Ríos,
dfernandez@facen.una.py
María Florencia Goberna,
gobernaflorencia@gmail.com

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Regulatory challenges and global trade implications of genome editing in agriculture

Danilo Fernández Ríos[1,2,3]*, Silverio Andrés Quintana[1], Pilar Gómez Paniagua[1], Andrea Alejandra Arrúa[1,3], Gustavo René Brozón[4], Moises Santiago Bertoni Hicar[5], Andrés Castro Alegría[2] and María Florencia Goberna[6]*

[1]Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Asunción, San Lorenzo, Paraguay, [2]Doctorado en Ciencias Agrarias, Universidad San Carlos, Asunción, Paraguay, [3]Grupo de Investigación Mycology Investigation and Safety Team, Centro Multidisciplinario de Investigaciones Tecnológicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, [4]Centro Multidisciplinario de Investigaciones Tecnológicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, [5]Unión de Gremios de la Producción, Asunción, Paraguay, [6]Coordination of Innovation and Biotechnology, National Bioeconomy Directorate, Sub-secretariat of Agricultural Production and Forestry, Secretariat of Agriculture, Livestock and Fisheries, Buenos Aires, Buenos Aires, Argentina

Genome editing revolutionized agriculture by improving crop productivity, disease resistance, and adaptation to adverse climatic conditions. However, it has faced significant regulatory challenges due to divergent regulations between regions. Although Europe classified these organisms as genetically modified organisms, Africa, Asia, and Latin America implemented more flexible regulatory frameworks, which encouraged innovation and the participation of small companies. These differences could generate high costs, delays in commercialization, and difficulties in product traceability, affecting research and development decisions. This article analyzes the main regulatory challenges and their impact on global trade, proposing strategies for regulatory harmonization to promote transparency, reduce trade barriers, and maximize the potential of these technologies in the face of global challenges such as food security and climate change.

KEYWORDS

genome editing, new breeding techniques, regulatory science, international trade, harmonization

1 Introduction

Genome editing technologies[1] have advanced significantly in recent years, expanding their applications in agriculture. These tools allow precise changes to the genetic characteristics of crops, favoring improvements in productivity, disease resistance, and adaptability to changing climatic conditions (Rajput et al., 2021; Zenda et al., 2021; Das et al., 2022; Ntsomboh-Ntsefong et al., 2023; Groover et al., 2024).

1 Refers to novel techniques for manipulating the genome with greater precision than that of pre-existing genetic engineering methods. These technologies have major implications for innovation across biomedicine, agriculture, and industrial biotechnology, owing to their more exact, less expensive, and easier genetic manipulation (Shukla-Jones et al., 2018).

However, their adoption faces significant regulatory challenges due to the diversity of existing policies at the global level. The regulations governing genome editing vary considerably among regions, which generates uncertainty and complexity for its implementation in international trade and agriculture (Tachikawa and Matsuo, 2023; Rosado, 2024).

In this article, we comment on the regulatory and trade challenges arising from these policy discrepancies, highlighting their implications and proposing strategies to promote greater global regulatory harmonization.

2 Regulatory landscape and challenges

The distinction between process- and product-based regulations represents a central axis in the governance of genome editing. In a process-based regulatory system, oversight is typically triggered by the use of recombinant DNA technology, rather than by the properties of the resulting organism. This approach originated in the early 1990s with a regulatory framework that distinguished conventional breeding methods (such as hybridization and mutagenesis) from genetic engineering involving the insertion of DNA (EUR-Lex, 1990). The term "genetically modified organism" (GMO) emerged to capture this technical boundary.

In contrast, product-based regulatory systems assess organisms based on the characteristics of the final product, regardless of the method used to generate them. Canada's regulatory model for "plants with novel traits" exemplifies this approach (Sprink et al., 2016). According to the Canadian Food Inspection Agency, a novel trait is defined as one that is new to the local environment and has the potential to affect a plant's safety for human health or the environment, regardless of whether it was introduced through genome editing, conventional breeding, or mutagenesis (Government of Canada, 1990; Canadian Food Inspection Agency, 2020).

This regulatory dichotomy has prompted scientific institutions to advocate for product-based, evidence-driven governance. The European Academies' Science Advisory Council concluded in 2013 that genetic engineering does not pose intrinsically greater risks than conventional breeding and advocated for a regulatory shift based on product traits rather than the methods (European Academies Science Advisory Council and Deutsche Akademie der Naturforscher Leopoldina, 2013). This view is supported by decades of empirical research showing that risk is associated with the function and expression of novel traits and not the mechanism of their introduction (Heap, 2013; Hartung and Schiemann, 2014; Sprink et al., 2016). In nature, similar genetic alterations occur spontaneously through mutations, recombination, or horizontal gene transfer, challenging the rationale for process-based oversight (Fernández Ríos et al., 2025). From a biosafety perspective, risk estimates for some products obtained through genome editing should thus align with those for naturally occurring genetic variation or conventionally bred plants (Hernández-Soto and Gatica-Arias, 2024).

Moreover, the enforcement of process-based regulations becomes technically unworkable when it cannot be determined whether a product was generated using a specific technique. For example, if a mutation produced by CRISPR/Cas cannot be distinguished from that arising through mutagenesis, then the ability to ensure compliance and implement policies for unapproved GMOs in seeds becomes functionally impossible. This outcome undermines the regulatory goals of traceability and safety assurance (Sprink et al., 2016). Although some scholars have argued against framing the debate as a binary opposition between process and product regulation (Kuzma, 2016) and call for more integrative approaches, it remains essential to recognize that product characteristics must ultimately form the basis for regulatory coherence and proportionality (McHughen, 2016).

Genome editing regulations vary considerably among regions (Figure 1), such as the European Union, Africa, Asia, and Latin America (Zarate et al., 2023; Sprink and Wilhelm, 2024). In the European Union, genome-edited organisms are currently classified as GMOs, although proposals to categorize certain edited products with a limited and predefined number of genetic changes in a differentiated manner are being evaluated (Ahmad et al., 2023; Purnhagen et al., 2023). Although pre-marketing requirements are not yet fully defined, they are likely to include measures such as labeling, segregation, and specific regulations for handling. Post-marketing requirements, such as additional monitoring, are also under discussion and may include more detailed regulations in the future.

However, more flexible regulatory approaches have been adopted in Asian countries, such as China and India. Since 2022, China has implemented regulations that shorten the approval times for products derived from new breeding techniques (NBTs) to 1–2 years. This framework prioritizes food safety and environmental impact assessments. Pre-market requirements include assessment processes similar to those applied to GMOs, whereas post-market provisions mandate labeling to ensure transparency and consumer awareness in the marketplace (USDA, 2023). Meanwhile, India has adopted a similarly flexible regulatory approach, excluding products developed through SDN1 (deletions or substitutions without adding foreign DNA) and SDN2 (using an exogenous DNA template but not integrating foreign DNA into the final genome) from being classified as GMOs, provided they do not contain foreign DNA. These products are exempt from biosafety assessments, and their status is certified by an Institutional Biosafety Committee, allowing them to be treated as conventional crops (Ministry of Environment, Forest, and Climate Change, 2022; Groover et al., 2024). This approach fosters innovation by reducing development costs and time and accelerates the commercialization of genome-edited products. India thus seeks to promote technological advances in agriculture (FAO, 2022).

On the other hand, in Africa, Burkina Faso, Ethiopia, Kenya, Nigeria, and Malawi are advancing toward adaptive regulatory frameworks for genome editing based on the principles of case-by-case review and risk proportionality. Kenya and Nigeria have developed guidelines that distinguish between conventional, intermediate, and transgenic products, applying different levels of regulation depending on the nature of genetic modification (Adegbaju et al., 2024; Groover et al., 2024). Both systems include early consultation mechanisms to determine the appropriate regulatory pathway, thereby providing greater clarity and predictability for developers. Ethiopia has drafted regulations excluding certain genome-edited products without foreign DNA,

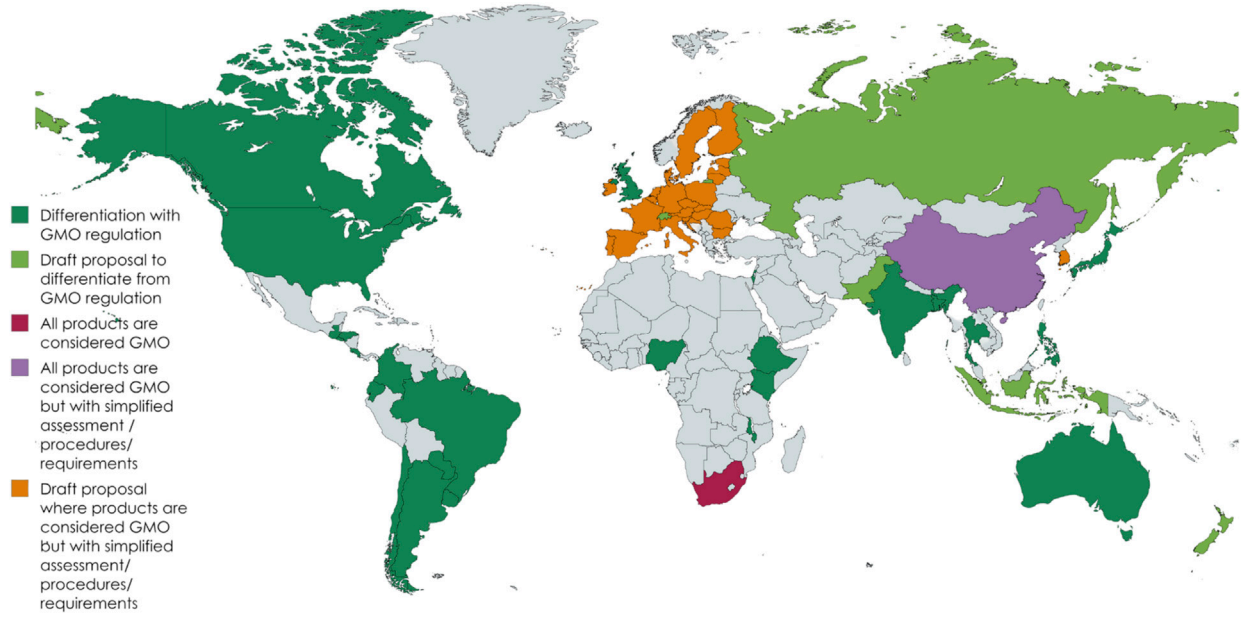

FIGURE 1
Global genome editing policy development.

with proposals currently under review (Groover et al., 2024). This growing trend positions Africa as an emerging reference point for the development of regulatory frameworks that combine scientific rigor with flexibility to facilitate responsible innovation (Rabuma et al., 2024; Akinbo et al., 2025).

On the other hand, regulations in some countries in Latin America establish prior consultation on whether a product derived from NBTs will be considered conventional or not, providing clarity and predictability from the early stages of development (Fernández Ríos et al., 2024; Hernández-Soto and Gatica-Arias, 2024; Pérez et al., 2024; Sánchez, 2024; Brant et al., 2025). If the final product does not contain foreign DNA or introduce a novel genetic combination—and could have been generated through natural processes—it is classified as a conventional product, which significantly reduces regulatory costs and opens up opportunities for small and medium-sized companies to participate. This framework also encourages the generation of more productive varieties adapted to market demands, boosting agricultural innovation and regional competitiveness (Lubieniechi et al., 2025).

Regulatory differences create barriers to the adoption of genome editing technologies, affecting the competitiveness and international trade of agricultural products. Table 1 presents a comparative summary of regulatory approaches in different regions.

3 Trade barriers and opportunities in genome editing

Regulatory discrepancies between regions affect the global trade of genome-edited products by increasing costs, delaying approvals, and reducing market access. Developers must navigate diverse regulatory frameworks, requiring adaptation to local rules and often additional testing, documentation, and procedures that vary by country. These challenges not only slow commercialization but also increase costs, limiting companies' ability to bring innovations to market efficiently. Small and medium-sized developers are particularly affected as they have fewer resources to meet multiple regulatory requirements and face greater barriers to entry (Kalaitzandonakes et al., 2023). In addition, regulatory uncertainty discourages investment in R&D as companies tend to prioritize crops with a lower risk of facing trade barriers (Lassoued et al., 2018). This could limit the potential of genome editing to address global issues such as food security and climate change.

On the other hand, variability in pre- and post-market requirements between regions raises concerns about transparency in the use of genome editing technologies. These disparities reduce the availability of information to consumers and complicate risk management in the global trade of agricultural products (Brinegar et al., 2017).

To address these challenges, experts recommend advancing regulatory harmonization mechanisms, drawing inspiration from successful models in countries where regulation focuses on the final product (May et al., 2022; Lassoued et al., 2024). Additionally, establishing bilateral and multilateral agreements could help align regulatory criteria and promote convergence.

4 Discussion

The global regulatory landscape for genome editing in agriculture is characterized by significant heterogeneity, ranging from strict process-based systems to more flexible product-based approaches. This diversity creates complex and often significant barriers to the advancement and adoption of genome editing technologies.

TABLE 1 Comparative overview of genome editing policies across countries and regions.

Region/Country	Regulatory approach	Reference
Argentina, Brazil, Chile, Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Paraguay, Ecuador, and Uruguay	Case-by-case assessment of products obtained through genome editing. If the final product does not have a new combination of genetic material, it is considered conventional	Fernandes et al. (2024), Fernández Ríos et al. (2024), Goberna et al. (2024), Hernández-Soto and Gatica-Arias (2024), Sánchez (2024)
Australia	Has revised its regulations to exclude SDN1 from oversight. Modifications without the introduction of foreign DNA not interpreted as additional risks	Thygesen (2019), Jones et al. (2024)
Bangladesh	Case-by-case approach. Products obtained through SDN1/SDN2, with no foreign DNA, excluded from strict regulations	Groover et al. (2024)
Burkina Faso, Ghana, Kenya, Malawi, and Nigeria	Guidelines using a case-by-case approach, excluding certain genome-edited products without foreign DNA from strict regulations	Adegbaju et al. (2024), Groover et al. (2024)
Canada	Applies product-based approach. Assesses final traits of the organism, not the technique used to develop it. Plants without foreign DNA are exempt from strict regulations[a]	Lassoued et al. (2024)
China	Regulation prioritizes food safety and environmental risk assessment. Pre-market requirements include risk assessment processes similar to those applied to GMOs, while post-market provisions provide mandatory labeling, thus ensuring transparency and traceability of products on the market	USDA (2023)
Ethiopia	Drafted guidelines exclude certain NBT products from strict regulations, still under the process of review and approval	Groover et al. (2024)
European Union	Genome-edited organisms considered GMOs. There are proposals to categorize certain edited products, with a limited and pre-defined number of genetic changes in a differentiated manner. Pre-market requirements not yet fully defined, likely to include labeling, segregation, and specific provisions for handling	Purnhagen et al. (2023), Molitorisová et al. (2024)
India	Products obtained through SDN1/SDN2, with no foreign DNA, not considered GMO	Ministry of Environment Forest and Climate Change (2022), Groover et al. (2024)
Indonesia and Vietnam	A draft has been proposed to exempt certain genome-edited products from strict regulations. Still under discussion, awaits implementation	Yang and Zhou (2024)
Japan	Case-by-case approach, excluding certain genome-edited products that do not contain foreign DNA from strict regulations	Tomita (2024)
Philippines and Singapore	Case-by-case approach, excluding products without foreign DNA from strict regulations	Groover et al. (2024)
Russia	It implemented a decision for a research and development program that classifies genome-edited products as similar to conventional products	Dobrovidova (2019)
South Africa	Considers NBT, including genome editing, such as GMOs	Berger, 2022; ACB (2024)
South Korea	Currently updating regulatory frameworks for NBTs. Currently, these techniques are regulated under the law on Living Modified Organisms (LMOs)	Yang and Zhou (2024)
Thailand	Exempts products obtained through SDN1 from strict regulations; for SDN2 and SDN3, without foreign DNA, assessment performed case by case to determine applicable regulation	Groover et al. (2024)
United Kingdom	Measures were implemented to allow field trials of genome-edited plants, requiring only one registration	Groover et al. (2024)
United States	Case-by-case approach. The Department of Agriculture and Environmental Protection Agency assesses products	Hoffman (2021), Groover et al. (2024)

(Continued on following page)

TABLE 1 (*Continued*) Comparative overview of genome editing policies across countries and regions.

Region/Country	Regulatory approach	Reference
	according to their competencies; the Food and Drug Administration offers voluntary consultations and does not require mandatory prior review	

[a]According to current genome editing regulations, any crop variety with herbicide tolerance will invariably be classified as a plant with a novel trait (Lubieniechi et al., 2025).

One primary barrier to innovation and competitiveness is the adoption of strict regulations in which all genome-edited organisms are classified as GMOs. This approach subjects genome-edited crops to the same approval processes as GMOs, regardless of whether foreign DNA is present in the final product or whether the genetic change could have occurred naturally or through conventional breeding. Such overly burdensome regulations increase the cost of bringing products to the market, reduce the returns on investment, and create investment uncertainty, which discourages innovation, especially from smaller developers and public research institutions. The time and resources required to navigate these complex regulatory pathways can divert efforts from R&D.

In contrast, regulatory frameworks adopted by some Latin American countries tend to be more innovation-friendly. When no foreign DNA is present in the genome-edited product and a change could have arisen through conventional breeding, these countries often exempt such products from GMO regulations. This streamlines the path to the market, provides greater regulatory certainty for developers, and encourages investment by reducing the likelihood of costly and time-consuming regulatory delays. Argentina's prior consultation instances (PCIs) exemplify how such frameworks can successfully facilitate agricultural innovation (Goberna et al., 2022; Goberna et al., 2024).

However, even with more flexible frameworks in some regions, the lack of international harmonization remains a significant obstacle. Differing regulatory requirements across countries can disrupt international trade, increase compliance costs, and delay the commercialization of new technologies, especially for smaller developers who must navigate a patchwork of regulations.

A lack of transparency, predictability, or a clear scientific basis in regulatory processes increases the risk for innovators, often discouraging investment in genome editing. Developers require science-based, transparent, and risk-proportionate regulations to invest confidently and bring genome-edited products to market.

Although genome editing holds great potential to address the United Nations Sustainable Development Goals, such as Zero Hunger, Good Health and Well-Being, Climate Action, and Life on Land, disjointed and inadequate regulatory frameworks can pose major challenges to biotechnological innovation (Jenkins et al., 2021; Robusti and Farina, 2025). Excessively strict process-based regulations, lack of international alignment, and regulatory uncertainty all contribute to higher costs, development delays, and reduced incentives for the adoption of genome-edited crops.

Concrete recommendations for regulatory convergence are urgently needed, given the limited number of genome-edited products currently available in the market. This early stage presents an opportunity to align frameworks before broader commercialization takes place. To strengthen the coherence and efficiency of genome editing oversight, we propose recommendations that regulatory authorities and harmonization initiatives can adopt.

The comparators used in regulatory evaluations should shift from the traditional focus on GMOs to those based on conventionally bred products (Hernández-Soto and Gatica-Arias, 2024). This adjustment would enable a risk-proportionate approach by aligning regulatory scrutiny with the characteristics of the final product rather than the method of genetic modification, thereby acknowledging the biological equivalence between certain genome-edited outcomes and those obtained using conventional techniques.

Administrative resolutions should explicitly classify genome-edited organisms as conventional when they do not contain foreign DNA or novel genetic combinations. This formal legal qualification enhances clarity across related regulatory procedures, including seed registration, labeling, and commercial authorization, while ensuring consistency with national and international biosafety frameworks.

Molecular characterization requirements should be limited to the species level when the edited trait falls within the range of natural or induced variation. Requiring varietal-level analyses in such instances imposes an unnecessary technical burden and risks regulatory disproportionality. A species-level focus provides sufficient resolution for compliance verification without impeding product development timelines.

Regulatory frameworks should incorporate formal recognition of prior determinations made by competent authorities in countries with compatible biosafety systems (Hernández-Soto and Gatica-Arias, 2024). Such decisions can serve as valid references for expedited assessments, facilitating regulatory convergence, improving efficiency, and reinforcing trust among jurisdictions without necessitating redundant evaluations.

A recent example of regulatory cooperation is the *Agências de Biossegurança em Rede para Biotecnologia* (ABRE-Bio) Memorandum of Understanding between Argentina and Brazil, which establishes institutional coordination between regulatory agencies to synchronize the evaluation and approval of agricultural biotechnology products (MECON and MCTI, 2022). This initiative aims to minimize regulatory asynchronies that could disrupt trade while ensuring safety for agroecosystems and food security at both national and regional levels. Benefits of this system include feasibility pre-assessment services for small and medium-sized developers without legal representation in destination markets, joint determination of the regulatory status of NBT-derived products, and significant reductions in regulatory timelines for all users (Secretaría de Agricultura, Ganadería y Pesca, 2023). Recently, Paraguay and Uruguay signed the agreement, and ABRE-Bio is open to any country interested in joining (Astarita et al., 2025; Lewi et al., 2025).

Similarly, in Australia and New Zealand, a joint food regulation system managed by Food Standards Australia New Zealand

(FSANZ) ensures that genetically modified foods, including those developed using genome editing, are assessed and approved under unified safety criteria before commercialization (FSANZ, 2025). This model offers a regional example of coordinated oversight that reduces trade barriers while safeguarding consumer health.

The New Partnership for Africa's Development (NEPAD) program represents a significant strengthening of national regulatory capacities for both GMOs and genome-edited products (AUDA-NEPAD, 2018; Rabuma et al., 2024). NEPAD has actively promoted regional harmonization of biosafety policies, fostering cooperation among Member States and integrating socio-economic assessments alongside environmental considerations as part of regulatory decision-making (Adegbaju et al., 2024). This approach positions the region as an emerging leader ready to adopt new agricultural technologies.

Finally, genome editing oversight should be grounded in a precise legal definition that invokes conventional breeding. Clarifying this legal boundary would enable more predictable decision-making, lower compliance costs, and promote equitable access to innovation across both the public and private sectors.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding authors.

Author contributions

DF: conceptualization, resources, project administration, investigation, validation, writing – review and editing, methodology, visualization, writing – original draft, formal analysis, software, data curation, supervision, and funding acquisition. SQ: data curation, investigation, software, methodology, visualization, validation, and writing – original draft. PG: investigation and writing – original draft. AA: resources, investigation, funding acquisition, writing – review and editing, and supervision. GB: writing – review and editing, data curation, and validation. MB: validation, writing – review and editing, and formal analysis. AC: investigation, validation, writing – review and editing, supervision, and writing – original draft. MG: formal analysis, investigation, writing – original draft, visualization, data curation, conceptualization, writing – review and editing, methodology, and validation.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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EDITED BY
Clara Rubinstein,
Institute for Scientific Cooperation in Environment and Health (ICCAS), Argentina

REVIEWED BY
Sandra M. Ruzal,
University of Buenos Aires, Argentina

*CORRESPONDENCE
Katherine A. Karberg,
katie.karberg@bayer.com

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The ever-evolving world of microbes: the current state of microbial taxonomy, genome evolutionary dynamics, and the potential impact on the future of agricultural microbials risk assessment

Katherine A. Karberg*

Bayer Crop Science, Chesterfield, MO, United States

Risk assessment frameworks for plant agricultural biotechnology products have been in place for decades, focused on the evaluation of living biotechnology products created through genetic engineering. These products contain genetic material from outside the breeder's gene pool, which is often from different taxa or represents "novel combinations of genetic material". These products are typically considered to be "genetically modified" (GM) organisms in regulatory jurisdictions. However, in the microbial world, particularly among Bacteria and Archaea, the rapid expansion of genome sequence databases shows that natural microbial innovation primarily occurs through the natural exchange of genetic material from various sources, even from different taxa. This means that many microbes can be considered naturally occurring GM organisms. This raises the question of whether labeling a microbe as GM is always scientifically relevant for risk assessment. In most regulatory frameworks, being classified as GM significantly impacts the registration path, especially for microbes intended for environmental release. A more effective and science-based regulatory approach would assess the actual functions of a microbe rather than relying on the uncertain classification of its genetic material. This would benefit regulators, developers, and society by promoting the use of microbial technologies for agricultural use.

KEYWORDS

agricultural biologicals, microbial genome evolution, horitzontal gene trasfer, microbial taxonomy, pangenome, regulation, risk assessment, biosafety

1 Introduction

Microbial biologicals have been used in agriculture since the turn of the 20th century; however, challenges related to consistent efficacy, stability, production scalability, and other obstacles have prevented them from becoming a primary tool in agricultural production (Batista and Singh, 2021; Debnath et al., 2020). Advances in basic microbiology knowledge and production capabilities, the need for novel and complementary approaches in modern crop production, and societal drivers on

sustainability collectively create an opportunity for the use of microbial biologicals. A limiting factor for realizing the potential of microbial biologicals is fit-for-purpose regulatory systems specific to the biological realities of microbes; especially for microbes with intentional genetic modifications, including the transfer and integration of genes from different taxa (EFSA Scientific Committee et al., 2020; Kerr and Bullard, 2020; Thakor and Charles, 2025).

Biotechnology regulatory systems have been in place and effective for plant biotechnology innovations since the mid-1980s (Gleim and Smyth, 2018). However, these systems are predicated on the idea that transfers of genes from outside the breeder's gene pool leading to "novel combinations of genetic material" (NCGM), particularly between different taxa, would not be naturally derived due to presumed natural barriers of gene transfer. This leads to the belief that such transfers represent a violation of "natural laws" and carry inherently greater risk. This plant biotechnology framework has thus far carried over to microbial biologicals. Accordingly, current risk assessment paradigms for microbial products with added gene content or other changes that categorize them as GM or NCGM are sometimes more intensive than those deemed as "conventional" or "wild type". This can present a financial barrier and significant increase in timelines to development, may restrict large scale field trials that are essential to demonstrate efficacy, and potentially rule out effective microbial solutions for farmers (Chemla et al., 2025).

In the time that global biotechnology risk assessment frameworks have been in place, the genomic era led to a rapid expansion of the sequence database across the tree of life which has increased the knowledge of microbial diversity and evolution. The analyses of bacterial and archaeal genomes have changed the "conceptual foundations of microbiology" (Koonin et al., 2021). Rather than fixed entities, most bacterial and archaeal genomes are now understood to be dynamic, with constant genetic flux (Arnold et al., 2022; Brito, 2021; Gophna and Altman-Price, 2022). Horizontal gene transfer (HGT), even between distantly related taxa, is the dominant mechanism of genetic innovation (Dmitrijeva et al., 2024; Sheinman et al., 2021). However, HGT dynamics remain an active area of investigation (Arnold et al., 2022; Brito, 2021). The abundance of microbial sequence data has also changed microbial taxonomic practices (Hug, 2024; Hugenholtz et al., 2021).

Many features of microbial evolution do not easily reconcile with current risk assessment frameworks that depend heavily on whether a microbe is designated as GM with genes acquired from different taxa or NCGM. The example of the *Paenibacillus* genus illustrates this point with its expansive genetic diversity and ever-evolving taxonomy. *Paenibacillus* is a diverse bacterial lineage long noted as a potential treasure trove for biotechnology uses in agriculture, human and veterinary medicine, bioremediation, and other industrial uses (Grady et al., 2016). This includes the use of whole *Paenibacillus* strains, known as microbial biologicals, as plant growth promoting bacteria in agriculture (Padda et al., 2017).

1.1 Microbial taxonomic practices are actively evolving

Taxonomic classification of microbes is an important, but evolving discipline (Hackmann, 2025; Hugenholtz et al., 2021; Oren et al., 2023; Riesco and Trujillo, 2024). The abundance of microbial sequence data has changed microbial taxonomic practices, leading to debates on consensus methods and the biological relevance of taxonomic ranks, including the longstanding debate over how to define a microbial species (Vernikos et al., 2015). The ongoing evolution of microbial taxonomy is critical for understanding the complexities of microbial life. However, it also directly impacts risk assessment frameworks, regulatory practices, and the effective application of microbial biologicals in agriculture and environmental management.

There are a variety of historical and current approaches for assigning microbial taxonomic ranks, but even those that propose consensus standards are often soon challenged by new research (Hackmann, 2025; Hugenholtz et al., 2021; Parks et al., 2018; Riesco and Trujillo, 2024). Initially, microbial taxonomy was based on phenotypic characterizations such as morphology, biochemical testing, lifestyle (e.g., pathogenic), and habitat (Hugenholtz et al., 2021). However, phenotypic approaches are limiting for elucidating evolutionary relationships, as distantly related microbes can have shared features, such as coexisting in a habitat or sharing metabolic capabilities such as nitrogen fixation.

The ability to compare genetic sequences was a critical paradigm shift for microbial taxonomy. DNA:DNA hybridization was one of the first methods to approximate genetic relatedness, followed by more comprehensive gene sequencing (Brenner, 1973). The discovery of the 16S rRNA gene as a slowly evolving, universally present non-eukaryotic microbial gene was a major step forward in microbial molecular phylogeny and led to the reframing of the tree of life into three different domains, including the discovery of the Archaea as a domain distinct from Bacteria and Eukarya (Woese and Fox, 1977). In the genomic era, taxonomic classifications now rely heavily on multi-sequence genome-based classifications, using metrics such as average nucleotide identity (ANI) to delineate species, supplemented by phenotypic information (Parks et al., 2020; Riesco and Trujillo, 2024).

However, at least 85% of microbial life is estimated to be unculturable and thus has no phenotypic information (Rinke et al., 2013). Sequence-based classifications allow for phylogenetic and taxonomic explorations into the uncultured realm, derived from metagenome-assembled genomes and single cell genomics. However, even if taxonomic ranks can be assigned based on sequence thresholds, there is no consensus on how to name such species according to the International Code of Nomenclature of Prokaryotes, as there is no representative physical sample to archive (Hugenholtz et al., 2021; Oren et al., 2023). That is, for most microbial diversity, there is no reference strain, no "wild type" or "conventional" counterpart, let alone consensus nomenclature for formally naming such species. As more genome sequences are added, a taxonomic system for uncultured microbes is resolved, and phylogenetic methods advance, further revisions of the tree of life are anticipated (Eme and Tamarit, 2024; Hug, 2024).

1.2 The microbial pangenome concept and its use in taxonomic classifications

Modern sequence-based taxonomic methods rely on sequence attributes that are held in common between organisms. However, there is significant genetic diversity even at the species level for many microbes. For example, *Escherichia coli* strains exhibit vastly different lifestyles, ranging from non-pathogenic lab, commensal, and environmental strains, as well as different pathogenic strains that cause significant human diseases. These variations arise from their different genetic content. For example, pathogenic *E. coli* strains have on the order of 300-1,000 more genes than the non-pathogenic ones (Rasko et al., 2008).

Extensive species-level genetic diversity permeates bacterial and archaeal lineages, leading to the pangenome concept (Medini et al., 2005). The total collection of genes in a lineage is the pangenome. The genes held in common are the core genome, typically representing operational genes for basic cell functions including DNA replication, transcription, and translation machinery. The remaining genetic diversity not held in common is the accessory (or variable, dispensable, auxiliary, amongst other names) genome. Accessory genes generally reflect functional adaptations to specific lifestyles, such as metabolic clusters, virulence factors, defense mechanisms, and more (Sheinman et al., 2021).

Core genes, due to their universal presence, are presumed to be vertically inherited making them reliable to construct phylogenies for taxonomic ranking (Hugenholtz et al., 2021; Parks et al., 2018). Yet, there is debate that using core genes are not sufficiently representative to define taxonomic ranks, because so much of the representative genetic diversity in a lineage, the accessory genome, is excluded, potentially missing additional cohesive forces that shape microbial genomes (Douglas and Shapiro, 2024; Zhu et al., 2019).

1.3 The dynamic nature of microbial accessory genes

The ever-increasing amount of sequence data reveals that for many microbial lineages the accessory genome contains more genes than the core genome, in the most extreme cases representing 80% of the lineage gene content (Tettelin and Medini, 2020). The current sequence database is not yet saturated for many microbial lineages, meaning that the gene pool at a given taxonomic designation continues to grow, expanding the accessory genome (Lapierre and Gogarten, 2009). This is referred to as an open pangenome.

Accessory genes are thought to often be acquired through HGT processes, rather than vertically inherited (Dmitrijeva et al., 2024). These genes often exhibit sequence characteristics (G + C content, codon bias) that are distinct from core genes. They may also be linked to chromosomal markers that indicate gene transfer, such as insertion sequence elements and integrated phage elements, or reside on extrachromosomal mobile elements such as plasmids, which facilitate their movement between different taxa. However, bacterial and archaeal genomes do not grow indefinitely; there is evidence that accessory genes are also often lost over time. Additionally, these genes can undergo adaptive mutations when they are integrated into new host organisms. As a result, accessory genes are particularly dynamic compared to core genes.

The evolutionary dynamics of HGT and the accessory genome are not fully understood, even though they make up a significant portion of the genes in many microbial lineages (Domingo-Sananes and McInerney, 2021). It is thought that genes transferred between closely related organisms are more likely to evade the host's defenses against "non-native" DNA, such as restriction-modification systems and CRISPR-Cas9. These closely related genes may also integrate more easily into the recipient's genome if they share similar features and functions. However, gene sharing is not limited to closely related organisms; it also occurs between distantly related lineages across taxonomic ranks, including examples of HGT between different domains of life, especially Bacteria and Archaea (Gophna and Altman-Price, 2022; Kloesges et al., 2011). Further, for some lineages, codon bias analyses of the accessory genome, and especially the most recently horizontally acquired genes, demonstrate that they are more similar to each other in codon bias than the core genes are, suggesting that they may be from a common gene pool that is shared beyond the genus level (Karberg et al., 2011). What, if any, implications a gene pool that extends across taxonomic ranks has on taxonomy remains to be determined. Regardless, much is still to be discovered about the dynamic nature of microbial genomes and what the vast genetic diversity in a lineage means for phylogeny and taxonomic designations.

1.4 The *Paenibacillus* genus illustrates the evolving nature of microbial genomes and taxonomy

The *Paenibacillus* genus, of great interest from a biotechnology perspective due to its diverse functional content, exemplifies the uncertainties in microbial taxonomy and genome evolution. Taxonomic revision within the *Paenibacillus* genus is common and ongoing (Grady et al., 2016). For nearly 100 years, strains were classified as members of the *Bacillus* genus based on basic phenotypic characteristics such as morphology, oxygen respiration, and endospore formation. However, more advanced biochemical and phenotypic analyses conducted in the late 1980s indicated the presence of distinct groups within these strains. In 1993, 16S rRNA gene sequencing confirmed the distinct groups, each proposed as novel genera, including the *Paenibacillus* genus (Grady et al., 2016). *P. polymyxa* was designated at the genus type strain in 1994, not because of its evolutionary or biological significance for the genus, but due to the historical circumstance of being one of the better characterized *Paenibacillus* strains at the time, having been cultured in 1880 (Pandey et al., 2023).

In the genomic era, the genetic diversity of *Paenibacillus* genus continues to expand. It is already expected that the genus will be reclassified into novel genera (Grady et al., 2016). There are also ongoing proposals for novel species, including a recent study of *P. polymyxa* strains supporting that the lineage be split into four different species based on genome sequence metrics, coupled with phenotypic data (Maggi et al., 2024). In this same study, a pangenome analysis revealed that even if the current strains are reclassified into four new species, each new species has an open pangenome. That is, the extent of the genetic diversity is not at saturation even at the species level of the type strain and the gene pool of *Paenibacillus* at any taxonomic rank cannot yet be defined.

1.5 The *nif* regions in the *Paenibacillus* genus are part of the accessory genome, are non-native, of variable organization, and are actively undergoing evolution in natural strains

A key focus of agricultural microbials is developing microbes to fix nitrogen in crops to reduce the need for synthetic fertilizers. Nitrogen fixation is energetically expensive, and microbes repress this pathway if sufficient environmental nitrogen is available (Fan et al., 2019). Even if microbes naturally possess such capabilities and have a symbiotic relationship with plants (legumes), they may not work efficiently in agricultural settings where synthetic nitrogen is already used. Precise engineering of this pathway in microbes has the potential to upregulate biological nitrogen fixation in typical agricultural settings, thus reducing the need for synthetic fertilizers (Wen et al., 2021).

Biological nitrogen fixation genes, including the *nif* genes, are part of the accessory (Xie et al., 2014). N-fixing genes in this lineage have variable organization, indicating that they are prone to significant evolutionary change. Nitrogen fixation is not an ancestral trait of *Paenibacillus*; rather it has been acquired through multiple HGT events from phylogenetically distant taxa. The donor for at least one of the *nif* HGT events is from *Frankia*, which belongs to a different bacterial phylum, Actinomycetota. Another donor of the nitrogen fixation genes appears to be from another domain of life, a methanogenic archaeon. This aligns with the evolving understanding of HGT, where gene transfer potential is influenced by the total gene pool in an ecological niche, even occurring between distantly related members (Arnold et al., 2022; Dmitrijeva et al., 2024).

The differential organization of the *nif* genes in *Paenibacillus* strains supports that evolution of the region is ongoing. The genes are organized into at least two different subgroups, with variation in gene organization and structure even within subgroups (Xie et al., 2014). This differential organization is the result of horizontal acquisition, gene loss (including total loss of the region in some strains), reacquisition of some *nif* and other functionally related genes, and additional sequence evolution, including changes in promoter regions.

2 Discussion

Advancing agricultural microbials requires regulatory systems with fit-for-purpose risk assessments that allow large-scale field trials to demonstrate efficacy. Currently, most global regulatory systems do not provide efficient pathways, if they exist at all, for commercialization of intentionally modified microbes, including those with genetic elements from different taxa or NCGM. Given the understanding that HGT is the main mechanism of microbial innovation, that gene pools and NCGM are not yet circumscribed because microbial sequence diversity is far from saturation, and the ongoing evolution of microbial taxonomy, it is necessary to reevaluate risk assessment frameworks based on these criteria.

HGT occurs across taxonomic ranks, including between different domains of life. Most microbes constantly sample and obtain genes from external sources, both cellular and acellular, then integrate, mutate, and lose them, using their own "genetic engineering" methods, similar to those used for intentional modifications. The scientific basis of risk assessment distinguishing acquired genetic elements by donor taxa especially must be revisited. A nitrogen fixation gene transferred between different bacterial phyla is not expected to have a different hazard profile than an intrageneric one, nor is it violation of "natural laws" if this is a phenomenon already found in nature.

Microbial taxonomy is also apt to change as the genome databases grow, the methodologies for comparing genomic information and deriving phylogenies advances, along with the knowledgebase of microbial evolutionary dynamics. The reality today is that the debate on a biologically relevant consensus definition of a bacterial or archaeal species is ongoing. In a regulatory context, if a gene is initially considered intrageneric is reclassified as intergeneric, does that change its hazard or the ethical ramifications of sourcing it?

For many microbial lineages, like *Paenibacillus*, the question of whether an engineered strain represents NCGM (including genes from other taxa) cannot accurately be answered, because the pangenome is open and the sequence databases are not at saturation. This means that the gene pool of the *Paenibacillus* genus is not yet circumscribed. The patchwork presence of nitrogen fixation pathway in some *Paenibacillus* strains illustrates several characteristics of the accessory pangenome. These genes are not fixed, and they experience gene gain from distant taxa, gene loss, and mutation to adapt to specific ecological roles. There is no definitive "wild type" or "conventional" version of the genes or pathway, and the availability of additional genome sequences continues to reveal NCGM. These concepts apply to other taxa that are of great interest as agricultural microbials, including *Bradyrhizobium* (Terra et al., 2025; Zhong et al., 2024).

Establishing a framework that ensures intentionally modified microbes can be safely used in agriculture is paramount. Furthermore, an objective, standardized safety evaluation of the final product should be the critical criteria, rather than focusing on the processes by which they were developed or on criteria that are subject to change. Microbes can be tested by a variety of methods, and potential strategies for biocontainment and reduction of other risks can be implemented, such as those recently described by Chemla et al. (Chemla et al., 2025). However, the testing should be fit-for-purpose for the intended use. For example, a non-animal-pathogenic microbe with modifications to the nitrogen fixation pathway would not be expected to have enhanced human pathogenicity, so a fit-for-purpose risk assessment may not require an extensive animal testing package; if information on animal pathogenicity were deemed necessary, safety information (in the form of literature searches on pathogenicity or lack thereof, or even preexisting animal data) can be bridged from a related strain.

Progress is ongoing in both the development of regulatory frameworks for agricultural biologicals and in the knowledge of microbial genetic diversity, genome evolutionary dynamics, and taxonomy. Even amidst new discoveries in the microbial world, the potential of innovative agricultural biologicals to address environmental and societal challenges can be realized if regulatory frameworks are anchored in objective criteria and testing methods.

Author contributions

KK: Conceptualization, Formal Analysis, Investigation, Project administration, Supervision, Writing – original draft, Writing – review and editing.

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Conflict of interest

The author KK is an employee of Bayer Crop Science, a manufacturer of crop protection products including microbial biologicals.

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EDITED BY
Monica Garcia-Alonso,
Estel Consult Ltd., United Kingdom

REVIEWED BY
Paul Keese,
University of Ghana, Ghana

*CORRESPONDENCE
Danilo Fernández Ríos,
dfernandez@facen.una.py
Andrés Castro Alegría,
andres.castro@usc.edu.py

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Naturally transgenic plants and the need to rethink regulatory triggers in biotechnology

Danilo Fernández Ríos[1,2]*, Nidia Benítez Candia[1], Silverio Andrés Quintana[1], María Florencia Goberna[3], Eva Nara Pereira[4], Andrea Alejandra Arrúa[1,5] and Andrés Castro Alegría[2]*

[1]Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Asunción, San Lorenzo, Paraguay, [2]Doctorado en Ciencias Agrarias, Universidad San Carlos, Asunción, Paraguay, [3]Coordinación de Innovación y Biotecnología, Dirección Nacional de Bioeconomía, Subsecretaría de Producción Agropecuaria y Forestal, Secretaría de Agricultura, Ganadería y Pesca, Buenos Aires, Argentina, [4]Departamento de Biología Molecular y Biotecnología, Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Asunción, San Lorenzo, Paraguay, [5]Mycology Investigation and Safety Team, Centro Multidisciplinario de Investigaciones Tecnológicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay

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1 Introduction

Horizontal gene transfer (HGT) is a widespread phenomenon across all domains of life, and has been a driving force of evolution (Keeling and Palmer, 2008; Boto, 2010; Wickell and Li, 2020). Viral sequences have been found in all eukaryotic (Liu et al., 2011; Gilbert and Cordaux, 2013; Takemura, 2020) and prokaryotic kingdoms (Schleper et al., 1992; Rambo et al., 2022), and HGT has been found to occur in all directions between kingdoms of the same domain (Nelson et al., 1999; Keeling, 2009; Fuchsman et al., 2017).

Plant species have stably integrated foreign sequences into their genomes. This natural transgenesis has occurred repeatedly in the evolution of plants, affecting their biology and genetic diversification (Ma et al., 2022). Some of the mechanisms of natural HGT have been characterized to sufficient extent to be used for genetic engineering applications, and the list of mechanisms of gene transfer mastered and applied to engineering might expand with the advancement of scientific knowledge. In order to make the case that natural HGT must be taken into account when designing regulatory frameworks for transgenic organisms, and in particular of transgenic crops, we will address the particular case of HGT from bacteria to plants.

The term "transgenic" usually refers in the literature to DNA constructs resulting from the process of gene transfer between species through genetic engineering (Gordon and Ruddle, 1981; Horsch et al., 1985). *Agrobacterium*[1]-mediated transformation has

1 The collective term *Agrobacterium* is used in recognition of tradition and due to the impossibility of precisely identifying the bacterium responsible for the plant transformation that occurred millions of years ago. The T-DNA fragments present in plant genomes are insufficient for this determination (Matveeva, 2021a). The classification of the genus is still evolving, as the taxonomic affiliation of five *Agrobacterium* genomospecies has not yet been determined, suggesting a possible increase in the number of species in the future (Flores-Félix et al., 2020).

established itself as the most widely used method for this purpose. In this procedure, a modified *Agrobacterium* plasmid transfers the desired DNA into the recipient cell, integrating it into its genome and allowing its hereditary transmission (Gelvin, 2009).

2 Horizontal gene transfer in plants

For stable incorporation of a sequence into a host organism and its transmission to offspring, certain conditions must be met. First, the foreign sequence must be integrated into the host genome. Then, the incorporated sequence must not be lost in the genomic rearrangements during cell divisions. In addition, the transformed cell must be part of the germline, to ensure inheritance. Finally, the integrated sequence must persist throughout evolution (Lacroix and Citovsky, 2016).

HGT is a process by which genes are transferred between unrelated organisms, as opposed to inheritance from parents. A clear example of gene acquisition by HGT is nitrogen fixation, a metabolic process present in certain bacteria of the genus *Paenibacillus* and regulated by the nif (nitrogen fixation) operon. These metabolic pathways are not specific to *Paenibacillus*, but have been acquired from phylogenetically distant organisms, including some of the Archaea domain and closely related bacterial phyla. HGT plays a key role in these changes, which has resulted in great diversity in the sequence and structure of nitrogen fixation regulatory elements, reflecting the multiplicity of such events from different donor organisms (Fuchsman et al., 2017). Although this phenomenon has been widely documented in Bacteria and Archaea, it has also been observed in eukaryotes, including plants (Keeling, 2024). In the latter, one of the most studied examples of HGT is the transfer of DNA from bacteria of the genus *Agrobacterium* to various plant species (Matveeva, 2021b).

Agrobacterium can transfer part of its DNA (T-DNA) to plant cells. Once incorporated, this T-DNA is integrated into the recipient genome, resulting in naturally occurring transgenic plants, or naturally occurring genetically modified plants (nGMs) (Matveeva and Otten, 2019). These plants have sequences in their genomes called cellular T-DNA (cT-DNA), homologous to *Agrobacterium* T-DNAs (White et al., 1983).

Most cT-DNAs identified to date appear to originate from *Agrobacterium rhizogenes*. However, cT-DNAs have also been found with previously unknown T-DNA sequences or unusual combinations thereof (Matveeva and Otten, 2019).

T-DNA sequences naturally transferred by various *Agrobacterium* species contain two types of genes, both regulated by promoters compatible with expression in eukaryotic cells. The first group of genes, called "oncogenes", encodes proteins that regulate the biosynthesis or response of plant cells to phytohormones, particularly auxins and cytokinins. Their expression causes uncontrolled cell division, leading to tissue proliferation and the formation of neoplastic growths, known as crown galls (De Cleene and De Ley, 1976; Lacroix and Citovsky, 2016). The second group of genes encodes enzymes involved in the synthesis of opines that can be used by *Agrobacterium* cells as a source of carbon and nitrogen (Lacroix and Citovsky, 2016). It has been proposed that for the emergence of a natural transgenic plant, two conditions must be met: the naturally infected plant must be able to regenerate from tissues transformed upon infection; and the structure of the incorporated T-DNA must allow or favor such regeneration (Otten, 2016).

3 Evidence of natural transgenesis in plants

HGT in plants was initially identified in species of the genus *Nicotiana*, in whose genomes the presence of *Agrobacterium* T-DNA was detected (White et al., 1983). Studies in *N. glauca* and *N. sylvestris* showed that bacterial DNA insertion was not an isolated event (Khafizova and Matveeva, 2022).

The identification of new cT-DNA sequences in several plant species has been possible thanks to whole genome sequencing databases. The evidence suggests that HGT from bacteria to plants is a more common phenomenon than previously thought and that it has occurred in multiple plant lineages (Bogomaz et al., 2024) (Table 1).

Genes acquired by HGT can retain their functionality in recipient plants and influence their traits. An example of this is *Ipomoea batatas*, where a cT-DNA has been identified with functional *Agrobacterium* genes which have remained stable over time (Kyndt et al., 2015). In addition, such genes can affect certain phenotypic traits, such as the *rol* genes, associated with root development (Quispe-Huamanquispe et al., 2017).

Unlike transgenics obtained through genetic engineering, in which genes are inserted in a targeted manner in the laboratory, nGMs acquired foreign DNA through natural infections (Chen and Otten, 2017). Between 5%–10% of dicotyledonous species are estimated to contain cT-DNAs (Matveeva, 2021b). With approximately 200 million species in this class, about 10,000 species would be nGM plants (Folta and Otten, 2021). The existence of nGM plants challenges the separation between "natural" and "artificial" made by regulatory triggers when determining which types of plants should be subjected to biosafety assessments, by showing that transgenics are not only the result of human manipulation, but also a naturally occurring phenomenon.

4 Discussion

The natural presence of *Agrobacterium* sequences in plant organisms questions the logic of strictly regulating transgenics obtained through genetic engineering, while exempting organisms that are similar, but obtained through conventional methods (Ammann, 2014; McHughen, 2016). cT-DNA evidence suggests that regulation focused on the method of production may be inadequate (Gould et al., 2022). In many regulatory frameworks, a transgenic organism is one that contains deliberately altered genetic material which does not occur "naturally" through breeding or selection (EFSA, 2024). This inconsistency becomes more evident when considering that the same trait can be obtained

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TABLE 1 Examples of nGM plants reported in the literature.

Family	Species	References
Apocynaceae	*Apocynum venetum*	Lipatov et al. (2022)
Burseraceae	*Boswellia sacra*	Matveeva (2021a)
Caprifoliaceae	*Lonicera japonica*	Lipatov et al. (2022)
	Lonicera maackii	Lipatov et al. (2022)
Caryophyllaceae	*Silene noctiflora*	Matveeva (2021a)
	Silene uniflora	Matveeva and Otten (2019), Matveeva (2022)
Convolvulaceae	*Cuscuta australis*	Zhang et al. (2020)
	Cuscuta campestris	Zhang et al. (2020)
	Cuscuta gronovii	Zhang et al. (2020)
	Cuscuta suaveolens	Zhang et al. (2020)
	Ipomoea batatas	Kyndt et al. (2015)
	Ipomoea trifida	Matveeva and Otten (2021)
Ebenaceae	*Diospyros lotus*	Matveeva (2021a)
Elaeagnaceae	*Elaeagnus angustifolia*	Lipatov et al. (2022)
Ericaceae	*Vaccinium corymbosum*	Matveeva (2021a)
	Vaccinium macrocarpon	Matveeva and Otten (2019), Zhidkin et al. (2023)
	Vaccinium microcarpum	Matveeva (2023)
	Vaccinium oxycoccos	Zhidkin et al. (2023)
Erythroxylaceae	*Erythroxylum cataractarum*	Zhidkin et al. (2023)
	Erythroxylum daphnites	Matveeva (2022)
	Erythroxylum densum	Lipatov et al. (2022)
	Erythroxylum havanense	Matveeva (2022)
Euphorbiaceae	*Triadica sebifera*	Matveeva (2022)
Fabaceae	*Aeschynomene evenia*	Matveeva (2021a)
	Arachis appressipila	Yugay et al. (2025)
	Arachis macedoi	Bogomaz et al. (2024)
	Arachis magna	Bogomaz et al. (2024)
	Arachis monticola	Yugay et al. (2025)
	Arachis paraguariensis	Bogomaz et al. (2024)
	Arachis pintoi	Yugay et al. (2025)
	Arachis pusilla	Bogomaz et al. (2024)
	Arachis rigonii	Bogomaz et al. (2024)
	Arachis stenophylla	Yugay et al. (2025)
	Arachis stenosperma	Bogomaz et al. (2024)
	Arachis trinitensis	Yugay et al. (2025)
	Arachis valida	Bogomaz et al. (2024)
	Arachis villosa	Yugay et al. (2025)
	Eperua falcata	Matveeva (2021a)

(Continued on following page)

TABLE 1 (*Continued*) Examples of nGM plants reported in the literature.

Family	Species	References
Kewaceae	*Kewa caespitosa*	Matveeva (2021a)
Myrtaceae	*Eucalyptus cloeziana*	Matveeva (2021a)
Molluginaceae	*Pharnaceum exiguum*	Matveeva (2021a)
Nyssaceae	*Nyssa sinensis*	Matveeva (2021a)
Paulowniaceae	*Paulownia fortunei*	Lipatov et al. (2022)
Plantaginaceae	*Linaria acutiloba*	Matveeva and Lutova (2014)
	Linaria dalmatica	Vladimirov et al. (2019)
	Linaria genistifolia subsp. *dalmatica*	Matveeva and Lutova (2014)
	Linaria vulgaris	Matveeva and Lutova (2014)
Rhizophoraceae	*Ceriops decandra*	Matveeva (2022)
Salicaceae	*Populus alba* × *Populus glandulosa*	Matveeva (2021a)
Solanaceae	*Nicotiana glauca*	Suzuki et al. (2002)
	Nicotiana noctiflora	Zhidkin et al. (2023)
	Nicotiana otophora	Matveeva and Lutova (2014)
	Nicotiana sylvestris	Matveeva and Lutova (2014), Khafizova and Matveeva (2022)
	Nicotiana tabacum	Suzuki et al. (2002)
	Nicotiana tomentosa	Matveeva and Lutova (2014)
	Nicotiana tomentosiformis	Matveeva and Lutova (2014)
Theaceae	*Camellia oleifera*	Lipatov et al. (2022)

both by genetic engineering techniques and by conventional breeding, creating different regulatory thresholds for products with the same traits.

These inconsistencies also extend to relevant aspects of risk assessment, given that HGT represents an important topic in the evaluation of GM plants. In regulatory practice, HGT is typically evaluated using a pathway-to-harm approach (OECD, 2023). However, to date, no empirical evidence supports HGT from GM plants to soil bacteria under field conditions (Badosa et al., 2004; Demanèche et al., 2011; Ma et al., 2011). Similarly, while humans and animals routinely ingest DNA from multiple biological sources, the likelihood of HGT from GM plant-derived DNA to gut microbiota or host tissues remains extremely low (Jennings et al., 2003; Netherwood et al., 2004; Sieradzki et al., 2013; Korwin-Kossakowska et al., 2016). A detailed assessment of the potential for HGT from GM plants to microorganisms is beyond the scope of this work. For further information, readers are encouraged to consult Philips et al. (2022) for a detailed review.

Given these complexities, the existence of nGM plants highlights the need for a product-based regulatory trigger in which biosafety assessment focuses on the traits and phenotype of the final organism rather than the process by which it was obtained (McHughen, 2016). This approach offers several important advantages over traditional process-based frameworks, particularly in the context of emerging breeding techniques. Focusing on the characteristics and potential risks of the final product ensures regulatory coherence and risk assessment proportionality, avoiding inconsistencies where crops with similar traits are subject to different oversight (Caccamo, 2023; Brookes and Smyth, 2024). Not all GMOs pose the same level of risk; some have well-characterized, low-risk profiles; just as not all conventionally bred crops are inherently safe. Conventional methods such as wide crosses, mutagenesis, or spontaneous mutations can also result in traits with biosafety implications, including increased toxicity, allergenicity, or invasiveness (McHughen, 2016). While these products are generally not subject to a complete risk assessment, they are often regulated at various stages of the production chain (registration for the crop, safety assessment for the byproducts).

A product-based approach enables regulators to focus their efforts on the actual risk presented by a crop rather than presuming risk based on the technique employed (Sprink et al., 2016). This logic has already been adopted in the case of NBTs by countries such as Argentina, Brazil and Canada, that exclude certain products developed through NBTs from GMO regulations when no novel combination of genetic material is present in the final product (Goberna et al., 2023; Fernandes et al., 2024; Lubieniechi et al., 2025). This aligns with risk assessment principles that prioritize the traits of the crop. It also allows for the inclusion of conventionally bred crops in biosafety assessments when they present novel or potentially hazardous traits, which process-based systems tend to overlook (Gould et al., 2022). Altogether, adopting a product-based

perspective would contribute to building a coherent, adaptable, and science-driven regulatory framework for novel organisms.

Author contributions

DF: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review and editing. NB: Data curation, Formal Analysis, Investigation, Methodology, Validation, Writing – review and editing. SQ: Formal Analysis, Investigation, Methodology, Writing – original draft. MG: Data curation, Methodology, Validation, Writing – review and editing. EN: Data curation, Methodology, Validation, Writing – review and editing. AA: Data curation, Methodology, Validation, Writing – review and editing. AC: Data curation, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review and editing.

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EDITED BY
Carmen Vicien,
University of Buenos Aires, Argentina

REVIEWED BY
George Tzotzos,
Marche Polytechnic University, Italy
Dalia Marcela Lewi,
Instituto Nacional de Tecnología Agropecuaria, Argentina

*CORRESPONDENCE
Muffy Koch,
muffy.koch@simplot.com

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One risk assessment for genetically modified plants

Muffy Koch*, Jaylee DeMond, Matthew G. Pence, Elena A. Schaefer and Gary Rudgers

Simplot Plant Sciences, J. R. Simplot Company, Boise, ID, United States

With over 30 years' experience conducting risk assessments for genetically modified (GM) plants, regulatory agencies that review the safety of GM plants understand the potential food, feed, and environmental risks associated with these products. This vast regulatory experience is underutilized when risk assessments for GM plants are repeated on a per-country basis. The redundancy in country-by-country reviews of the same GM plants places a disproportionate regulatory burden on developers and strains limited government resources for conducting safety reviews. Requiring repeated, multi-country risk assessments to obtain food and feed import permits or cultivation permits for GM plants is unnecessary as repeated assessments do not change the safety and associated risks of already approved products. To avoid redundancies in the regulation of GM plants, we propose adoption of one, global risk assessment for food, feed, and environmental release carried out to international standards. Our proposed model for one global risk assessment encourages the sharing of food, feed and environmental risk assessment summaries between countries while maintaining national approvals for GM plants. Steps towards a streamlined and efficient review process for GM plants are discussed, including implementing a global, forward-looking approval process that eliminates repetitive risk assessments and re-reviews of low-risk traits. Harmonization of risk assessment is an achievable goal that would accelerate regulatory approvals and enable broader access to the benefits of GM plants which are currently only available to some countries.

KEYWORDS

GMO, low risk, regulatory efficiency, RNA interference, vegetative crops, cisgenes

Introduction

As we enter the fourth decade of genetically modified (GM) plants being approved and used internationally, regulatory experience with environmental risk assessments for cultivation approvals, and food safety risk assessments for food and feed approvals should be applied to remove unnecessary pre-market regulatory requirements and broaden market access for safe and beneficial products of biotechnology. Global harmonization of risk assessments for GM plants is an achievable goal that would accelerate regulatory approvals and expand access and deployment of safe and beneficial agricultural products with the potential to secure the food needs of an increasing world population (Koch et al., 2024). Streamlining the regulatory process for GM plants will improve equitable access to the technology for small developers, the public sector, farmers, and consumers. The Organization for Economic Cooperation and Development member countries have been working on global harmonization of environment, food and feed safety reviews for many years and have published a range

of consensus reports to guide countries as they set up review standards for GM plants (OECD, 2006; 2015). In addition, others have proposed a core set of studies to support food and feed safety assessments globally (Waters et al., 2021) and encouraged the streamlining of data requirements for environmental risk assessments (Anderson et al., 2021). We expand on these ideas with a model for implementing shared risk assessments and proactive approvals.

Countries with regulatory frameworks that are actively reviewing and making timely decisions on the food and feed safety of GM organisms generally follow the CODEX CAC/GL 45-2003 guidelines (FAO/WHO, 2009). As part of the review process, regulators consider safety data collected on new GM plants and identify potential hazards associated with consumption of food and feed products made from these plants. GM plants are compared to conventional plants that already have a history of safe use. Food and feed biosafety reviews take into consideration how the composition of a new event (event = a unique plant-trait combination) may impact the nutrition of products derived from it, the potential for changes in toxicity or allergenicity, changes to levels of endogenous antinutrients, and whether the modification changes how the plant will be used for food and feed. For any identified potential hazard, reviewers assess the likelihood of harm, the consequences should harm occur, mechanisms to manage risk, and whether the overall risk is acceptable in terms of a country's national protection goals.

Environmental safety reviews focus on how a new trait could potentially impact a GM plant's biology compared to conventional plants, and evaluate changes to invasiveness, weediness, persistence, gene flow to sexually compatible plants, and impacts on non-target organisms (OGTR, 2013). For identified, potential environmental hazards, a similar risk assessment as for food and feed considers the likelihood of harm, the consequences should harm occur, mechanisms to manage risk, and whether the overall risk is acceptable in terms of national protection goals.

Experience with safety assessments of GM plants has confirmed that potential risks to the environment or to human or animal health are identifiable and manageable in approved plants (Radin, 2003; Sanchez, 2015). At least 645 GM events have been reviewed for cultivation, food and feed safety in 46 countries (ISAAA, 2024). In most instances, the initial environmental, food and feed safety reviews were completed in the country where the plant was developed, first introduced to farmers, and placed on the market. In an unnecessary abundance of caution, the same food and feed safety reviews for GM plants are repeated in many countries where food and feed from the GM plant will be imported. Re-review is unnecessary to establish that an already approved GM plant is safe for human and animal consumption. Experience tells us that a single, well-constructed review is able to identify potential risks in a newly developed GM plant.

Once the safety has been determined for an approved plant-trait combination, repeated reviews are not needed and are costly for developers and regulators, delay deployment of previously approved GM plants, restrict developers, and limit farmers' access to improved planting material. An industry study determined that the cost of developing and commercializing a new GM plant was US$ 115 million and 38% of this cost, US$ 43 million, was for regulatory approvals (AgbioInvestor, 2022). For agencies that charge for regulatory reviews, the fees can be from US$ 5,000 to US$ 450,000, but costs agencies accrue to conduct GM risk assessments are likely higher.

We discuss ways to reduce this unnecessary regulatory burden and provide a model for moving ahead with a more streamlined, equally safe and efficient one global risk review of GM plants. In addition, examples are provided of low-risk GM plants where one environmental and one food and feed assessment are also sufficient for cultivation approval in many release environments and for human and animal consumption.

One global food and feed risk assessment

The data requirements for food and feed risk assessments are clearly defined and universal (Waters et al., 2021), therefore, once food safety has been determined, a global risk assessment summary could be used to eliminate additional food and feed reviews and inform food and feed approvals in all other countries.

Section 3 in Annex 3 of the CODEX guidelines (FAO/WHO, 2009) encourages member states to share risk assessment and safety information to facilitate food import approvals in other countries (FAO/WHO, 2009). Vietnam took an early step towards a global food and feed safety approval when they introduced a 2014 policy to accept the food safety of a GM plant that had food safety approval from five developed countries (Ministry of Agriculture and Rural Development, 2014). In 2013, Health Canada (HC) and Food Standards Australia and New Zealand (FSANZ) began collaborating on food safety risk assessments to streamline the review process for new GM plants in acknowledgement that food safety in one country is applicable in other countries (FSANZ, 2024). Bangladesh, Bhutan, India and Sri Lanka have been in discussion since 2020 about harmonization of food and feed safety assessments across these four countries (AFSI, 2025).

A review of approvals listed in the International Service for the Acquisition of Agri-biotech Applications (ISAAA) GMO Approval Database indicates that many events have had multiple reviews in multiple countries and by many agencies (ISAAA, 2024). After food safety reviews of 645 GM events in 46 countries, the learnings from these reviews need to be applied to simplify and modernize global reviews for food safety. For example, the maize event, MON810, was approved early in the development of GM crops and has 25 food approvals, 20 feed approvals, and 14 cultivation approvals listed in the ISAAA database (ISAAA, 2025), in addition to many more approvals as a stacked event that was bred together with other approved maize events. We cannot say whether the subsequent approvals identified unique country-specific safety concerns, but ultimately the many reviews did not change the first findings that the GM maize was safe for cultivation, food and feed use.

There may be instances where additional potential hazards are identified when the initial food and feed risk assessment is reviewed in another country. In this case the agency can focus their risk assessment on this concern, considering the pathway to harm, likelihood, consequences and risk management options for the new hazard without the need to reassess the previously reviewed hazards. For example, food consumption patterns or novelty of a food may require additional review in some countries. This

TABLE 1 Global regulatory approvals for GM potato events.

Construct	Event name	Global approvals per event[a]		Global reviews per construct
		Environment	Food/Feed	
pSIM1278	E12	2	9	32
	F10	2	5	
	J3	2	5	
	V11	2	5	
pSIM1678 (+pSIM1278)	X17	3	10	42
	Y9	3	10	
	Z6	3	6	
	W8	3	4	
pSIM4363	BG25	1	3	4
Totals		21	57	78

[a]All reviewed and approved for food and feed. Eight approved for cultivation in United States and Canada.

happened in the 1990s in South Africa with review of the MON810 maize event for general release approval. United States consumption data do not accurately reflect consumption in South Africa where maize is the staple food and consumed at much higher levels. United States maize consumption is estimated at 2.85 g/person/day (EPA, 2014), nearly eight times lower than the South African *per capita* consumption of 222 g/person/day (Ranum et al., 2014). The scientific review committee asked the applicant to provide exposure data for the South African population. Importantly, in this example the review committee identified the potential higher exposure that was not addressed in the application and asked for specific data to address that gap. This expedited the food review by focusing only on new potential hazards.

In our experience, following the approval of nine potato events in the United States, subsequent food and feed safety reviews in other countries have not identified any additional potential hazards (Table 1). The pSIM1278 construct is present in eight potato events. Collectively, the safety of the traits in pSIM1278 has been independently assessed and approved in 54 regulatory reviews by 10 agencies in nine countries (United States: Food and Drug Administration (FDA); Canada: HC and Canadian Food Inspection Agency (CFIA); Mexico: Federal Commission for the Protection against Sanitary Risk; Japan: Ministry of Health Labor and Welfare, Ministry of Agriculture, Forestry, and Fisheries; Philippines: Bureau of Plant Industry; Australia/New Zealand: FSANZ; Malaysia: Department of Biosafety; Singapore: Singapore Food Agency). Since the initial food and feed safety assessment by the FDA in 2013, none of the subsequent 53 reviews identified any new potential hazards or raised additional safety concerns regarding these traits in potatoes. These cumulative evaluations have consistently affirmed the safety of the traits and have not added or subtracted from the safety of the events. These events included five potato varieties, six different traits, and one selection strategy. Even with the diversity in genomic backgrounds and traits, no new safety concerns were identified in any of the subsequent reviews undertaken by food importing countries.

This is evidence that the repeated food safety reviews by importing countries do not increase the safety of the products. Instead, these redundant reviews confirmed the functionality of the initial review that was based on the CODEX guidelines. For potatoes, as these same traits are transformed into additional potato varieties, the current country-by-country review process will generate even more redundant risk assessments until a more science based approach to risk assessment is adopted globally.

One global environmental risk assessment

Data requirements for environmental risk assessments are defined clearly and are transportable across countries (Anderson et al., 2021; M. Bachman et al., 2021). While countries differ in their geographical locations and environments, it is not necessarily the case that one global environmental risk assessment would have little value due to environmental differences. Findings of invasiveness, weediness, gene flow, persistence, and impact on non-target organisms in the first country can be used to inform risk assessment in subsequent countries. The risk assessment findings from the initial review will need to be reviewed in subsequent countries, and this can be done with the help of local crop, trait and biodiversity experts without the need for in-country studies or additional data from developers/applicants. Using problem formulation methodology, these experts can identify whether novel pathways to harm are likely and focus any additional assessments on clearly defined, country-specific risk hypotheses that were not addressed in the initial review (Wolt et al., 2010). Importantly, while plant performance is environment-specific, the performance of a plant is not a safety consideration in a regulatory approval.

In cases where regulatory agencies determine traits introduced into GM plants are low risk, one global risk assessment for environmental release should also be feasible. Three decades of

environmental safety review of GM plants confirm that some categories of GM events are low risk across many environments.

Low-risk traits

Three categories of introduced traits have developed a history of safe use in edible crops, have been applied widely in commercial GM plants, and are recognized as safe by regulatory authorities. Examples of low-risk traits include those conferred using RNA interference (RNAi), retransformation of additional varieties of approved vegetatively propagated GM plants, and the use of cisgenic traits that are inserted into sexually compatible plants. These three groups of GM plants are discussed in more detail.

RNA interference

RNA interference involves the processing of endogenous double stranded RNA (dsRNA) into small RNA (e.g., miRNA, siRNA, etc.) to regulate gene expression in cells. This mechanism is common in plants, insects, fungi, nematodes, and animals (Shabalina and Koonin, 2008; Wilson and Doudna, 2013). Analysis of plant transcriptomes indicates that dsRNA are abundant in plants, with over eight million long dsRNA predicted in just five conventional crops: corn, soy, rice, lettuce, and tomato (Jensen et al., 2013). These naturally abundant dsRNA are processed by the plant into approximately 29 million unique small RNA with 100% complementarity to over 1,500 human transcripts (Ivashuta et al., 2009; Jensen et al., 2013; Frizzi et al., 2014). A diverse population of small RNA has been identified in conventional potato tubers (Zhang et al., 2013). This enormous diversity of endogenous small RNA is consumed regularly by humans and animals without incident. While there have been attempts to demonstrate that small RNAs from plants are capable of regulating human gene expression when humans are exposed to RNA from the consumption of plant-based foods, these findings are based on poor experimental design or misinterpretation of results (Pastrello et al., 2016).

Based on the universal presence of nucleic acids in the cells of every living organism, including every plant, animal and microbe used for food or feed, there is a long history of safe consumption of RNA and DNA. In 1998, the FDA reached a conclusion, stating that nucleic acids are "generally recognized as safe" (57 Fed Reg. 22984, 22990, 29 May 1992), and noting that "Introduced nucleic acids, in and of themselves, do not raise safety concerns. Thus, for example, the introduction of a gene encoding an anti-sense RNA would not raise concerns about either the gene or the anti-sense RNA. Any safety considerations would focus on the intended effects of the anti-sense RNA" (FDA, 1992). In 2001, the United States EPA established an exemption from the requirement for a tolerance for residues of nucleic acids (40 C.F.R. 174.507) under the Federal Food, Drug, and Cosmetic Act, noting that "nucleic acids are ubiquitous in all forms of life, have always been present in human and domestic animal food, and are not known to cause any adverse health effects when consumed as part of food" (66 Fed. Reg. 37817, 19 July 2001). The GRAS status of RNA has been relied on by United States Department of Agriculture (USDA) in regulatory decisions (USDA, 2006; 2011). In 2013, Food Standards Australia New Zealand, which evaluates food safety requirements from biotechnology foods, stated, "There is no scientific basis for suggesting that small dsRNA present in some GM foods have different properties or pose a greater risk than those already naturally abundant in conventional foods" (FSANZ, 2013). The history of safe use of nucleic acids, including small RNA, was based on its presence and safe use in all plants, including all plants that are used for food by humans.

Through naturally occurring evolutionary processes during plant adaptation and the use of traditional breeding practices, many plants and conventional cultivars contain inverted repeats because of genetic rearrangements. These are expressed as dsRNA, interact with Dicer to produce siRNA, and regulate expression of endogenous genes using RNA interference (Parrott et al., 2010; Petrick et al., 2013). Soybean seed color, maize stalk color, and rice protein content are examples of RNAi-based traits obtained through conventional breeding (Kusaba et al., 2003; Tuteja et al., 2004; Della Vedova et al., 2005).

Food and feed derived from approved GM plants using RNAi-based gene regulation is expected to be as safe for consumption as food and feed derived from conventional breeding (Petrick et al., 2013). From 1994 to 2022, over 30 RNAi-based events were approved by regulators for food, feed, or cultivation in alfalfa, apple, bean, maize, papaya, plum, potato, soybean, squash, and tomato. Approximately 242 (ISAAA, 2022) food and feed approvals exist in over 20 countries for RNAi-based events (ISAAA, 2022). These risk assessment decisions demonstrate that products with RNAi-based traits are considered safe for human and animal consumption, and subsequent safe consumption of these events in food and feed confirms that these findings are correct. Based on 242 food and feed approvals, approved GM plants with introduced RNAi-based traits should be considered as not needing country-by-country rereview within the proposed globally harmonized risk assessment model.

Retransformation of vegetative varieties

Vegetatively propagated plants such as banana, citrus, cassava, potato, and strawberry differ from sexually propagated or seed grown plants. For example, soybean and maize produce seed through sexual recombination (meiosis) resulting in progeny that are genetically and phenotypically different from their parents. Conversely, vegetatively propagated plants are genetically identical to their parent and have not undergone meiotic recombination or segregation. For this reason, vegetatively propagated plants are considered genetically stable (UPOV, 2002) and when plants such as potato are uniform, they can also be considered stable without need for additional stability testing (UPOV, 2004).

Simplot's GM potato products provide an example where agency conclusions concerning the safety of a GM vegetatively propagated crop remained consistent after subsequent reviews (Pence et al., 2024). Simplot has 78 approved petitions for commercial GM potato events globally (Table 1). Of these submissions, the three traits in the pSIM1278 construct have been approved 74 times (Table 1). No hazards were identified in these independent reviews.

In recognition of this unnecessary strain on time and resources, some regulatory agencies have implemented retransformation policies to address regulatory redundancy and the low risk of subsequent events. The Canadian Food Inspection Agency's Directive 94-08 "*Assessment Criteria for Determining Environmental Safety of Plants With Novel Traits*" (Section 5.4; CFIA, 2017) defines retransformation as "a transformation of a plant with the identical construct(s) as a previously authorized plant of the same species" and gives the developer the opportunity to notify the agency of the retransformed plant instead of undergoing the full determination process. The retransformed plant must meet three criteria: the traits are expressed in a similar range to the previously authorized plant; it is known, based on characterization, that the plant does not display any additional novel traits and is substantially equivalent to the previously authorized plant in terms of its use and safety; and novel food and feed requirements are met as appropriate. The CFIA's notification process is an efficient and streamlined process that does not compromise the environmental safety of the product.

A similar approach is recommended for all approvals of new traits in vegetatively propagated plants. Experience supports extending the approval for one event to all subsequent events in the same crop with the same traits. This will reduce the regulatory applications for agencies and developers without decreasing the safety of cultivation and use of these GM plants. Retransformation of new events of vegetatively propagated GM plants would not need repeated risk assessments within the proposed globally harmonized risk assessment model.

Gene insertions that mimic plant breeding—cisgenic plants

Cisgenic plants result from the introduction of genes from the same or closely related species and are often regulated under the same GM frameworks as transgenic plants. Schouten et al. (2006a) coined the term cisgenic plant nearly two decades ago and advocated for exemption of these plants from traditional GM regulations (Schouten et al., 2006b; 2006a; Jacobsen and Schouten, 2008).

The introduction of cisgenes through biotechnology has significant advantages compared to traditional breeding methods, especially for polyploid and vegetatively propagated plants. In potatoes, for example, true potato seed is not planted for commercial production because the genetic variability in the seed results in variable offspring with widely different characteristics and properties compared to the original parents. As a result, conventional plant breeding is not efficient for moving new traits into potatoes. To maintain the commercial quality traits that consumers, growers, and processors have come to expect from specific potato varieties, commercial potatoes are vegetatively propagated.

Maintaining genetic clones over years, decades, and even a century, as in the case of the Russet Burbank potato variety, comes at a cost. Pathogens, such as those causing late blight, often evolve rapidly and can overcome natural disease resistance in plants resulting in susceptibility to disease.

Although some wild and cultivated potato varieties possess naturally occurring plant resistance genes (R-genes), which provide resistance to late blight, breeding these traits into commercial potato varieties is time-consuming, labor-intensive, and often involves the transfer of undesirable traits. As an example, one attempt to breed the late blight R-gene *Rpi-blb2* from the wild potato species *Solanum bulbocastanum* into cultivated potato, took breeders 46 years (Hermsen, 1966; Hermsen and Ramanna, 1973; Haverkort et al., 2009). The resulting varieties, Bionica and Toluca, are used only on a limited scale because various agronomic and quality traits are not optimal for certain purposes (Jo et al., 2016).

Cisgenic approaches, by contrast, allow breeders to introduce desired genes from wild or crossable species into commercial varieties without disrupting other important agronomic or quality characteristics. More importantly, this can be accomplished in shorter time than the decades it takes for traditional breeding, while maintaining the desired traits of the variety. This approach has been used successfully to improve disease resistance in both vegetatively propagated plants including potato and apple (Vanblaere et al., 2011; Haesaert et al., 2015; Lazebnik et al., 2017) and polyploid plants including wheat and barley (Holme et al., 2012; Maltseva et al., 2021).

As our understanding of plant genetics and breeding advances, there is increasing recognition that regulatory oversight should prioritize the novelty and risk of traits rather than the technology used to introduce them. In particular, genetic insertions involving cisgenes should not be subjected to heightened regulatory scrutiny if those same genes feasibly could be introduced through conventional breeding methods. The European Food Safety Authority (EFSA) acknowledged that the introduction of cisgenes using biotechnology is at least as safe as conventional plant breeding (EFSA Panel on Genetically Modified Organisms, 2012). This approach is scientifically sound and represented by regulatory policy for cisgenic plants in agencies, such as HC, CFIA, U.S. Environmental Protection Agency (EPA), UK Department for Environment, Food and Rural Affairs (DEFRA), Food Standards Agency (FSA), and other national regulatory authorities (Health Canada, 2022a; CFIA, 2023; Environmental Protection Agency, 2023).

Health Canada and CFIA regulate novel food and plants with novel traits, respectively, emphasizing the novelty and potential environmental or health risks posed by the trait, regardless of how the trait was introduced and taking into account whether foreign DNA remains in the plant (Health Canada, 2022b; CFIA, 2023). These regulatory frameworks are intentionally process neutral. Importantly, when a cisgenic trait is introduced through biotechnology that could have otherwise been achieved via conventional breeding, and the trait itself is not novel in terms of food, feed, or environmental exposure, HC and CFIA may not consider the food, feed, or plant to be novel and will regulate the product as they would a conventionally bred plant.

In 2023, the United States EPA published a final rule exempting certain cisgenic plant incorporated protectants (PIPs) (Environmental Protection Agency, 2023). Under the Federal Insecticide, Fungicide, and Rodenticide Act, EPA regulates pest protection traits resulting from the introduction of genetic material into plants, which they refer to as PIPs. The 2023 rule

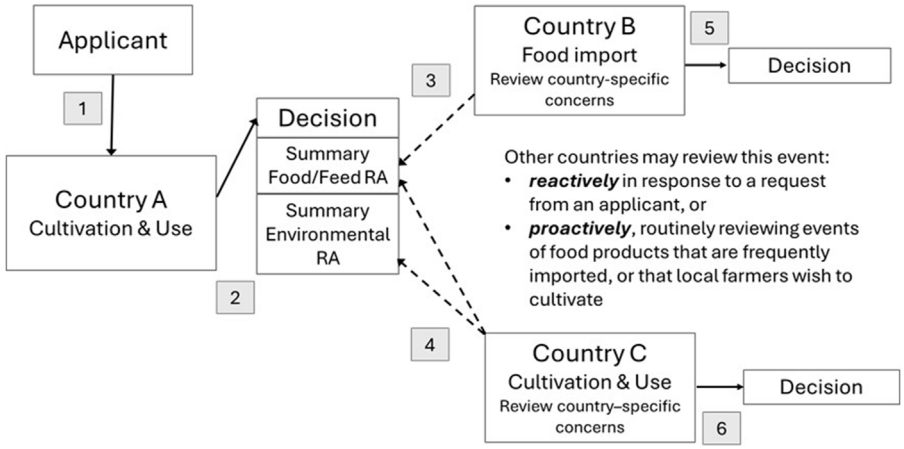

FIGURE 1
Proposed Model for Global Risk Assessments of GM Plants. Steps in the model are 1. Applicant applies for cultivation and use in country of first release, Country A. 2. Country A reviews the dossier and reaches a decision, posting risk assessment (RA) summaries on their website. 3. Food import Country B can access the food/feed RA summary from Country A and consider any additional hazards not already reviewed. 4. Country C, wishing to cultivate and use the GM plant, can access both food/feed and environmental RA summaries from Country A and consider any additional hazards not already reviewed. 5. Country B issues a decision on food safety. 6. Country C issues a decision on cultivation and use.

exempts a PIP active ingredient if it is a characteristic of the population of sexually compatible plants, is created through genetic engineering from either an insertion of a native gene or a modification of an existing gene in the recipient plant, the substance is identical in sequence to the substance in the source plant, and the inserted regulatory regions are identical to those in the source plant (Environmental Protection Agency, 2023).

These examples illustrate the evolving perspective of regulatory agencies on cisgenes derived from sexually compatible species, however, more progress is needed. The EPA's regulation maintains "genetic engineering" as the trigger for exercising its regulatory authority, focusing on the process used rather than the product resulting from the change. In addition, one factor that could inhibit developers from using this cisgene exemption is the presence of short segments of DNA used to introduce the gene of interest, such as *Agrobacterium* left and right border sequences, or short intervening sequences used during construct development. It can be argued that non-coding, non-expressed DNA sequences associated with cisgenes pose no additional risk and should be exempt from the EPA regulations.

It would be valuable for developers and farmers if more governments and regulatory authorities would categorize cisgenic traits as conventionally bred traits based on the evidence of the safety of these cisgenic changes in plants. This pivot would reflect a science-based approach that evaluates the risk of the product, and not the process by which it was developed, and would fit into a framework of global regulatory approvals, where traits based on cisgenes have been reviewed and demonstrated to be safe. Agencies like HC, the US EPA, CFIA and FSA have taken steps in the right direction. There is an opportunity now for regulatory authorities in other countries to revise regulatory policies that are not risk based, thus identifying cisgenic traits as low risk and good candidates for one global harmonized risk assessment.

Proposed model for global risk assessments

The proposed model for global risk assessments (Figure 1) is designed to minimize regulatory duplication while maintaining a high level of safety. This model maintains country sovereignty for decision making and encourages sharing of risk assessment summaries so that reviews in subsequent countries can focus on country specific potential hazards that were not previously assessed. In this model, after the first review and decision, other countries may review a GM plant reactively in response to a request from an applicant, or proactively by reviewing events for food products that are frequently imported or that local farmers wish to cultivate.

Countries may need to review their local regulatory policy to enable use of risk assessment summaries from other countries for national decisions. In some cases, country policy already lends itself to this process, for example, when regulation focuses on the safety of the product and not on the process used to develop it. In countries where there is a requirement for a formal applications to trigger a review, policies would need to be revised, and specific data requirements may need to be broadened to enable use of risk assessment summaries from other countries. The model does not stipulate what data are required, instead it relies on the outcome of a sound risk assessment using established risk assessment methodology.

Food and feed risks are universal, as are most environmental risks, however, some traits may raise concern unique to some countries. In this case, the national regulatory authority would identify the specific concern and outline a potential pathway to harm (Wolt et al., 2010). When using a global risk assessment summary, regulators use the biology of the conventional plant as the baseline for assessing risk. Once the biology of a plant is understood for the local environment, the impact of the added traits can be assessed to identify any new potential risk. This concern would be provided to the developer to address prior to decision making in that country.

Importantly, outside of regulations for pre-market review of GM plants, the safety of all food and all planting material is already regulated in countries. Implementing global GM plant regulatory processes does not impact the ability to review the safety of a product, nor detract from national public health regulations for food safety and plant pest regulations for environmental impact of conventional plants.

Discussion

This paper considers the experience regulators have developed with safety reviews for GM plants in the last four decades and proposes a progressive change in how these plants are regulated internationally. The proposal is for one food and feed and one environmental risk assessment summary that will be available to all countries for national decision making. These two risk assessment summaries would be the product of the first country approval. While not all countries issue risk assessment summaries, enough countries make these available to enable the one review model to work.

The model proposed here expands on an earlier proposal for the identification of a core set of studies to support food and feed safety assessments globally (Waters et al., 2021). Using data from one country, these studies could be applied across all countries for risk assessment. These authors concur that problem formulation could be used to identify unique hazards on a country-by-country basis. Our experience, obtaining regulatory approvals for potatoes, suggests that not only are the data requirements between regulatory agencies already harmonized, but the first risk assessment with the harmonized data would be sufficient for all countries to reach national food and feed safety decisions.

Similarly, this model expands on an earlier proposal to simplify and modernize the data requirements for environmental risk assessment of GM plants (Anderson et al., 2021). There is already alignment on environmental protection goals across many countries, making the alignment of data requirements and data transportability across countries an easy step in harmonization of environmental risk assessments (Garcia-Alonso et al., 2014; Nakai et al., 2024). The model presented here suggests that the first environmental risk assessment is applicable to most countries for local decision making. Some countries may identify country-specific potential environmental hazards that need additional data and risk assessment, but no additional safety is achieved by repeating the review of the hazards already addressed in the initial assessment.

While regulatory cooperation and harmonization preserve national sovereignty, their implementation demands sustained political resolve. The AFSI, 2025, whitepaper for advancing regional cooperation on agricultural biotechnology regulation states "Regulatory cooperation and harmonization do not compromise domestic autonomy but do require political will to implement." Several examples of harmonization across countries have emerged. Through the Health Canada-FSANZ Shared Assessment Process, applicants seeking food use of their biotech product for use in Canada, Australia, and New Zealand can submit an application to Health Canada and FSANZ. The food assessment is prepared by one of the agencies and then shared with the other. This risk assessment sharing is functioning and results in time and resource saving benefits for the agencies, improved efficiency in the authorization process, faster authorization times, and cost saving for the applicant. The Memorandum of Understanding, between Argentina, Brazil, Paraguay, and Uruguay, is another example of how countries can cooperate in regulatory assessments, while also maintaining domestic autonomy (Ministerio de Economia, 2025). As these examples evolve, they will serve as models for other countries and regions. Importantly, countries do not need MOUs to implement the model proposed here. Countries can make unilateral decisions to accept existing regulatory risk assessment summaries for GM plants they deem to have no additional risk for local conditions.

Reasons for a country to conduct further review would include country-specific information that raises a new potential hazard or an identified hazard in a new release environment, however these types of cases should be rare and based solely on traits that would pose identifiable and clearly documented risks. In particular, approved products that have been on the market for years, and which are cultivated safely in the environment, and consumed safely by humans and animals, likely would not require re-review.

The regulatory improvements suggested in this model also incorporate regulatory trends to extend approvals from one event to subsequent events with the same traits in the same crop, and to widen approvals for low risk traits. Evidence shows that approved RNAi-based crops and cisgenic crops pose no change to risk that is different from conventional, already-used food crops. Many regulatory agencies have recognized the safety of RNAi and cisgenes, especially when the traits could arise through traditional breeding. This alignment and a shift toward product-based, risk-proportionate oversight rather than process-based regulation, reflects current science and supports innovation. Similarly, reassessing vegetatively propagated crop varieties with the same trait or traits that have already been approved for food and environmental safety, has not identified new risks. The repeated reviews slow innovation, and result in unnecessary time and cost spent by both developers and governments.

Practical considerations

There are several practical considerations that would contribute to a successful global risk assessment strategy for GM plants (Table 2). Global harmonization of risk assessment for GM plants is possible if the practical considerations described in Table 2 are implemented with a focus on process improvement and identified risk. Technology that has the potential to address global challenges of climate change and food security could be accessed more broadly if regulators spend less time reviewing products with proven low risk and demonstrated safety.

Benefits

The benefits of single global regulatory food, feed and environmental risk assessments are numerous (Table 3). For all regulatory agencies, access to global environmental or food and feed risk assessment summaries would reduce time required for reviews and the need for specialist knowledge. Using established international standards for food, feed and environmental risk assessments will ensure scientific and objective safety reviews that are universally applicable. National agencies would review the safety summaries and make decisions for local approvals after taking into consideration local conditions, priorities, and protection goals. Access to risk assessment summaries would allow countries to

TABLE 2 Practical considerations for implementing one global risk assessment for a GM plant.

Consideration	Option
National sovereignty	Ensure that decisions to approve the use of a new GM plant remain a national obligation. In this model, the primary food and feed or environmental risk assessment objectively defines the safety of new GM plants and is used by national regulatory authorities to make national decisions for cultivation and use
First approval	Currently, cultivation approvals are submitted in the countries where the plants will be grown and food and feed submissions in countries that import products likely to contain the approved GM material. Under a one global risk assessment scenario developers are likely to submit the first application for a new GM plant to an agency that is science-based, functional, efficient, and cost effective
Separation of environmental safety and food and feed safety concerns during reviews	In our experience, countries that struggle to make efficient food and feed safety decisions often mix environmental safety into food and feed safety reviews (Koch et al., 2024). For efficient risk assessment, it is important to undertake review of food and feed safety separately from environmental safety. These reviews have different considerations, functions, and end points. As such, they should be considered separately. For example, a request for food and feed approval for imported nonviable food products does not need to consider issues like weediness and gene flow that might be important for a cultivation approval
Access to the primary risk assessment summary	Some agencies provide risk assessment summaries on their regulatory websites, making these available to other countries, such as trading partners, wishing to review the plants as they are approved. Agencies that produce publicly accessible risk assessment reports include the CFIA, FSANZ, European Food Safety Authority (EFSA), and the United States Department of Agriculture (USDA). Other regulatory agencies or countries can begin to think about ways to leverage these summaries in their own review and decision-making processes
Regulatory decision making	If, in reviewing a risk assessment summary from another country, an agency identifies a country specific potential environmental or food and feed hazard not considered in the first review, they could ask the developer for additional information on this specific hazard, without the needed to repeat the full environmental or food and feed biosafety review

TABLE 3 Benefits of access to regulatory risk assessment summaries for GM plants.

Beneficiary	Benefit
Regulatory agencies	Reduce time required for reviews
	Focus on country-specific potential hazards
	Reduce the need for knowledge specialists
	Provide confidence that the reviews were conducted scientifically and objectively
	Make national decisions based on country specific protection goals
	Eliminate duplicate reviews of low-risk and familiar traits
Countries	Enable proactive national approvals linked to farmer, consumer, and local business needs without formal applications for GM plants Access to improved planting material will:
	• Improve sustainable food production
	• Mitigate food shortages
	• Build agricultural and horticultural economies
Developers	Eliminate the cost of multiple submissions to additional countries
	Redirect regulatory funding to product development
	Reduce time to market
	Eliminate duplicate reviews of low-risk and familiar traits
Public sector and small developers	Leverage regulatory experience in national agencies for faster approvals and lower regulatory costs
Farmers	Increased access to diverse planting material with desired traits and sustainable production benefits to protect farms and produce
Commerce	Strengthen agricultural and horticultural sectors of the economy
Consumers	Access to safe and affordable food
	Adoption and acceptance of GM foods and agriculture

TABLE 4 Actionable recommendations for implementing global risk assessments.

Responsibility	Actionable recommendation
National regulatory agencies responsible for reviewing and approving GM plants	Based on the model, identify policy changes allowing implementation of a process to leverage the use of another country's risk assessment summaries to reduce regulatory redundancy
	Make risk assessment summaries and decisions available on regulatory websites. These records of the hazards identified and assessed are key to enabling adoption of global risk assessments for GM plants
	In making decisions, consider widening the approval, where scientifically sound, to future varieties of the plant with the same traits. This is particularly true for RNAi traits and any retransformation of vegetatively propagated plants with the same traits
	Revise policy to treat GM plants with cisgenic traits as conventional varieties derived from plant breeding. Focus on regulating the product rather than regulating the technology used in development
National representatives of member countries at the United Nations Food and Agriculture Organization (FAO) and World Health Organization (WHO)	Work together to review and update the CODEX guidelines for Foods Derived from Modern Biotechnology (FAO/WHO, 2009). After more than 30 years, safety assessment guidance should be updated to align with the vast experience of regulators. Consider all the recommendations in this paper, the recommendation on unintended effects from the Canadian regulators (Schnell et al., 2015) and the recommendations on genetic stability in vegetatively propagated plants during clonal propagation (Pence et al., 2024)

approve new GM plants proactively in response to national needs without receiving formal regulatory applications.

For public sector and small developers, one environmental and one food and feed safety review would eliminate the cost of multiple submissions to additional countries. In our experience, this cost saving can be millions of dollars, funding that could be used on development and safety assessments for additional products, rather than on duplicated submissions and risk assessments that do not add to the safety of already approved products.

Long term benefits for farmers and consumers would be increased access to diverse planting material with desired traits. This access could help improve sustainable food production and mitigate food shortages around the world. In time, wider use of safe GM products could help to normalize the use of GM plants.

Actionable recommendations

Actionable recommendations arising from this regulatory risk assessment proposal are listed in Table 4.

Conclusion

Decades of experience with risk assessments and approvals of GM plants have identified areas where regulatory efficiencies are possible without reducing the safety of GM products. Global access to environmental, food and feed risk assessment summaries from the first approval of a GM plant would remove the redundancy of numerous duplicated risk assessments in countries that subsequently review the plant for local cultivation or food import. With access to risk assessment summaries, countries can review these food, feed and environmental risk assessments and focus their risk assessment on unique potential hazards not previously reviewed. Maintaining national decision making, ensures that the final approval of GM plants remains the responsibility of each country. In addition, expanding approvals for GM plants with RNAi or cisgenic traits and to subsequent events of vegetatively propagated plants with the same traits, is supported by the low risk associated with these modifications. We encourage national regulatory agencies to implement this model which will reduce their reviewing time without compromising safety. This will provide benefits to developers by reducing regulatory redundancy, to farmers by facilitating increased access to improved planting material allowing more sustainable food production, and to consumers by providing access to high quality, affordable food.

Author contributions

MK: Conceptualization, Writing – original draft, Writing – review and editing, Supervision. JD: Writing – review and editing, Writing – original draft. MP: Writing – review and editing, Writing – original draft. ES: Data curation, Writing – review and editing. GR: Writing – original draft, Writing – review and editing.

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EDITED BY
Carmen Vicien,
University of Buenos Aires, Argentina

REVIEWED BY
Gerald Epstein,
RAND Corporation, United States
Gijs A. Kleter,
Wageningen University and Research, Netherlands

*CORRESPONDENCE
Drew L. Kershen,
dkershen@ou.edu

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Agricultural biotechnology in the courts: judicial opinions and commentary

Drew L. Kershen*

Earl Sneed Centennial Professor of Law Emeritus, University of Oklahoma, Norman, OK, United States

Seven jurisdictions from around the world have issued judicial opinions that address fundamental issues about the governance and regulatory systems of agricultural biotechnology. This article summarizes these legal proceedings and describes their impact upon agricultural biotechnology. The article then provides a commentary and critique of the legal proceedings and resulting judicial opinions.

KEYWORDS

agricultural biotechnology, breeding, environment, human health, litigation, judicial opinions, plant scientists

Introduction

Many courts around the world have issued judicial opinions about agricultural biotechnology. This author considers seven opinions, from seven different jurisdictions, as the most significant and consequential. In chronological order of issuing the opinion, these seven jurisdictions are New Zealand, the European Union, Kenya, Ghana, the Philippines, South Africa, and the United States. Each of these opinions decided whether modern techniques of molecular biology would be allowed or disallowed for crop breeding and crop improvement within that jurisdiction. These opinions also affect agricultural trade, though trade is not a significant focus of this article. Effectively, these opinions were deciding the future of agriculture for that jurisdiction. More broadly, each of these opinions is an important influence for the global debate about the future of agriculture.

In Part One of this article, the author presents a summary of the litigation and judicial opinions. The author then provides an impact analysis of these opinions for going forward with agricultural biotechnology in that jurisdiction. Finally, the author explains the present status, as of May 2025, of agricultural biotechnology and its food and feed products for each of these seven jurisdictions.

In Part Two, the author writes a commentary about these judicial opinions. The author critiques each of these judicial opinions and explores, from his pro agricultural biotechnology perspective, the deeper meanings and implications of these judicial opinions.

Part One: seven jurisdictions: litigation summary, impact, and present status

New Zealand

In October 2012, Scion, the Crown Research Institute for forest resources, applied to the Environmental Protection Agency (EPA) for a determination that forest plants created

using Zinc-Finger Nuclease Type 1 (ZFN-1) and Transcription Activator-Like Effector Nucleases (TALENS) were exempt from the Hazardous Substances and New Organisms Act of 1996 (HSNO 1996). Section 2 of HSNO 1996 included genetically modified organisms as new organisms subject to the 1996 Act. Section 3 of HSNO 1996 gives a list of organisms that are not genetically modified and thus not subject to HSNO and the implementing EPA regulations. Among those organisms exempted included organisms from "chemical or radiation" treatments (chemical or radiation mutagenesis). Scion argued that ZFN-1 and TALENS were similar to (equivalent to) chemical mutagenesis and, as set forth in HSNO Section 3 and the EPA regulations, created organisms not genetically modified.

After considering information supplied by Scion, considering objections to the application supplied by the Sustainability Council of New Zealand Trust, and after carefully reading the language of HSNO 1996, the EPA staff recommended to the EPA's governing HSNO Section 26 Committee that Scion's application be denied. [The Section 26 Committee is the deciding authority under HSNO 1996.]. The EPA staff focused on the facts that these two techniques used *in vitro*, laboratory, modern molecular biology to make genetic changes. In the opinion of the EPA staff, these facts made Scion's forest plants "new organisms" subject to the HSNO 1996 law and implementing regulations.

The EPA's governing Section 26 Committee considered the same information as the staff and the staff's recommendation. The Section 26 Committee decided that ZFN-1 and TALENS were similar to chemical mutagenesis. In fact, the Section 26 Committee determined that the mutations from ZFN-1 and TALENS would be indistinguishable from mutations occurring naturally or from chemical mutagenesis. The governing Committee concluded that Scion's forest plants thereby came within Section 3 exemption to HSNO 1996. Consequently, Scion would be able to conduct field trials and, ultimately, to release its forest plants into New Zealand without being required to pass through the strict regulatory regime HSNO 1996 established.

The Sustainability Council sought judicial review of the Section 26 Committee's decision by filing a lawsuit in the High Court, the trial court level, of New Zealand (Wellington Registry). The case name is *The Sustainability Council of New Zealand Trust against The Environmental Protection Authority* (Kershen, 2015).

In its opinion (The Sustainability Council, 2014), the High Court carefully and extensively discussed the technology issues and the various techniques for causing genetic mutations in plants. When the High Court finished this plant-breeding discussion, the High Court turned to competing interpretations of the statute (HSNO 1996) and the EPA regulations implementing the statute. The High Court's decision can best be summarized by quoting from two paragraphs in the opinion.

> "[66] A common feature of each of the techniques [the Section 3 list of exempt organisms] is that they were in common use at the time of the regulations. It makes sense that the regulations would exempt techniques that were well understood and established. There is less likely to be scientific and technical uncertainty about the effects of such techniques. It would therefore be consistent with the Act's purpose and the precautionary principle to exempt such common techniques rather than subjecting them to the approval regime of the Act. . . . it would follow that new techniques . . . were not intended to be included in the exemption."

And the quotation from the second paragraph is:

> "[73] For all these reasons, I consider the correct interpretation is that put forward by the Sustainability Council. That is, reg 3(1)(b) exempts organisms that are generated from organs, tissues or cell culture using any of the following techniques: selection and propagation of somaclonal variants, embryo rescue, cell fusion (including protoplast fusion), and chemical or radiation treatments that cause changes in chromosome number or cause chromosome rearrangements. It follows that the Authority [i.e., the Section 26 Committee] erred in its interpretation of the regulation because it considered that the regulations did not set out an exhaustive list and that techniques that are comparable and sufficiently similar to those listed in the Regulations should also be excluded."

The High Court interpreted Section 3 of HSNO 1996 as stating an exhaustive list of exempt organisms. As ZFN-1 and TALENS are not on the Section 3 exhaustive list of exempt organisms, organisms created by these unlisted techniques are subject to HSNO 1996. The High Court therefore granted relief to the Sustainability Counsel and rejected Scion's application. Under the High Court's opinion, Scions plants must pass through the strict regulatory regime HSNO 1996 established.

There was no appeal from the High Court decision, making it binding upon the legal system of New Zealand.

The detrimental impact upon agricultural biotechnology was immediate. After 2014, initiation of field trials of plants created through modern molecular biology (e.g., gene-editing techniques) ceased. Plants created through modern molecular biology do not exist in the agricultural sector of New Zealand because they are illegal and prohibited unless these plants have passed through the stringent regulatory procedures the HSNO 1996 established. As far as the author knows, since 2014, no plant breeder has even applied to the EPA for approval for a field trial or commercial release because the process for gaining approval is so burdensome and the likelihood of success is so small as to make the effort not worthwhile (USDA-GAIN NZ, 2023).

By contrast, Food Standards Australia New Zealand (FSANZ) has approved many food ingredients from genetically modified and gene-edited crops. While these food ingredients are listed on product labels as genetically modified, the author understands that New Zealand food stores carry a goodly number of these FSANZ-approved foodstuffs and that consumers calmly purchase these foodstuffs. Animal feeds made from genetically engineered and gene-edited crops are regularly and widely imported and commonly used by animal agriculture (USDA-GAIN NZ, 2023).

In New Zealand, the way-forward for agricultural biotechnology is through legislative and regulatory action. In December 2024, the Government of New Zealand introduced to Parliament a Gene Technology Bill. The Government says the objective of the Bill is to establish a new regulatory regime for genetically modified and gene-edited organisms that is: risk-proportionate (tiered regulatory

oversight based on product risk, not process); efficient in application and timely in decision-making; flexible to accommodate technological and policy developments; and aligned with international and Maori obligations. As of May 2025, the Health Committee of the NZ Parliament is holding public hearings on the Gene Technology Bill (Gene Technology, 2024). Significant legislative actions remain to occur before, if ever, the Gene Technology Bill would become the law of New Zealand.

The European Union

On 29 July 2013, Confédération paysanne, a French agricultural union, joined by eight other French environmental organizations, asked the French Minister of Agriculture to oppose the development of herbicide-tolerant crops. When the Minister of Agriculture did not satisfy their request, Confédération paysanne formally wrote the French Prime Minister, in December 2014, to ban the cultivation and marketing of herbicide tolerant (HT) canola varieties. These HT canola varieties came into existence through plant breeding techniques that are grouped together under an umbrella term of new genomic techniques (NGTs). When the Prime Minister declined to do so, on 12 March 2015, Confédération paysanne applied to the Council of State, France for a court order mandating the Prime Minister to ban these NGTs canola varieties (Confédération paysanne timeline, 2015). (The Council of State, France is the highest court for administrative justice within the French legal/judicial system.).

Due to the importance of the case for European Law, the Council of State, France referred the legal matter to the Court of Justice European Union (CJEU). [Bobek, 2018, ¶¶ 24–37]. This referral resulted in the CJEU docketing the first legal case in the EU related to gene-edited plants: Confédération paysanne against Prime Minister (2018) [Confédération paysanne 2018].

After docketing and under the procedures of the CJEU, the Court does not act until it receives an advisory opinion from the Office of the Advocate General about how to resolve the legal questions before the Court. Advocate General Bobek issued the advisory opinion on 18 January 2018 (Bobek, 2018).

In the advisory opinion, Advocate General Bobek opined that undefined terms, such as "mutagenesis" in the EU Directive 2001/18/EC, must be dynamic in interpretation so that the law can properly react to technical and social evolution. Otherwise, AG Bobek wrote,

> "The suggestion that the interpretation of such notions ought to be 'frozen' in the factual or societal circumstances that prevailed when those notions were passed into law would represent a singularly *originalist* approach to legal interpretation, not frequently encountered on this side of the Atlantic." [Bobek, 2018, ¶ 100, italics in the original.]

Based on this dynamic interpretative approach, AG Bobek concluded,

> "The exemption laid down in Article 3(1) of Directive 2001/18, read in conjunction with its Annex IB, covers all organisms obtained by any technique of mutagenesis, irrespective of their use at the date of the adoption of that directive, on the condition that they do not involve the use of recombinant nucleic acid molecules or genetically modified organisms other than those produced by one or more of the methods listed in Annex IB." [Bobek, 2018, ¶168].

On 25 July 2018, the CJEU issued the first judicial opinion in the EU on the legal status of gene-edited plants. The CJEU rejected the advisory opinion of AG Bobek and adopted an originalist approach to the interpretation of Directive 2001/18. Confédération paysanne against Prime Minister (2018) [Confédération paysanne 2018]. Quoting from the judicial opinion, the CJEU decided:

> "[51] . . . Article 3(1) of Directive 2001/18, read in conjunction with point 1 of Annex IB to that directive, cannot be interpreted as excluding, from the scope of the directive, organisms obtained by means of new techniques/methods of mutagenesis, which have appeared or have been mostly developed since Directive 2001/18 was adopted. Such an interpretation would fail to have regard to the intention of the EU legislature, reflected in recital 17 of the directive, to exclude from the scope of the directive only organisms obtained by means of techniques/methods which have conventionally been used in a number of applications and have a long safety record.

> "[52] That finding is supported by the objective of Directive 2001/18, as is apparent from Article 1 thereof, in accordance with the precautionary principle, to protect human health and the environment. . . ." [Confédération paysanne 2018, ¶¶ cited in the text quotations].

After the CJEU decision of 2018, the case returned to the Council of State, France to determine which specifically-identified mutagenic techniques (first) have been conventionally used in a number of breeding applications and (second) have a long safety record of use prior to the year 2001. On 7 February 2020, the Council of State, France ordered and decided,

> ". . .ordered the Prime Minister to determine . . . the restrictive list of techniques or methods of mutagenesis which have conventionally been used and have a long safety record. The Counsel of State considered, in [the 7 February 2020 decision], that both the techniques or methods of 'directed mutagenesis' or 'genome edition' and the techniques of '*in vitro*' random mutagenesis appeared or were mainly developed after the date on which Directive 2001/18 was adopted and must therefore be considered to be subject to the obligations imposed on GMOs by that directive . . ." [Szpunar, 2022, ¶16].

Thus, in its 7 February 2020 decision, the Council of State, France ruled that three mutagenic techniques (directed mutagenesis, gene-editing, and *"in vitro"*) are subject to the EU Directive 2001/18. By contrast, the Council of State also ruled that *"in vivo"* techniques are conventional techniques with a long history of safety and, thus, outside of the regulation EU Directive 2001/18.

The Council of State, France notified its decision to distinguish "*in vivo*" mutagenesis from "*in vitro*" mutagenesis to the EU

Commission. [Szpunar, 2022, ¶18]. This notification gave rise to the second EU judicial opinion related to mutagenic plant breeding techniques. The second case is Confédération paysanne against Prime Minister, 2023 [Confédération paysanne 2023].

In accordance with standard procedures, the CJEU did not act until it had received an advisory opinion from the Advocate General. Advocate General Szpunar issued the advisory opinion on 27 October 2022. In the advisory opinion, Advocate General Szpunar pointed out that the EU Commission, based on advice from the European Food Safety Authority (EFSA) and other Scientific Committees, dissented from the Council of State's distinction between "*in vivo*" mutagenesis and "*in vitro*" mutagenesis because the molecular mechanisms are the same, the types of mutations are the same, and "*in vitro*" techniques have been used since the 1960s and widely used since the 1990s [Szpunar, 2022, ¶¶ 45–56]. Based on these facts, AG Szpunar advised that CJEU should rule that random mutagenesis "*in vitro*" should be legally the same as random mutagenesis "*in vivo*" and, therefore, exempt from Directive 2001/18 related to GMOs. [Szpunar, 2022, ¶ 70].

On 7 February 2023, the CJEU ruled that "*in vitro*" random mutagenesis is exempted from the GMO Directive 2001/18 because this technique has conventionally been used in many breeding applications prior to 2001 and had a long safety record with regard to its use. The CJEU 2023 opinion rejected the Council of State, France distinction between "*in vivo*" mutagenesis and "*in vitro*" mutagenesis. [Confédération paysanne 2023, Rule after ¶ 67]. The CJEU ruled that "*in vivo*" and "*in vitro*" breeding techniques are legally equivalent. As legally equivalent, the CJEU decreed that both *"in vivo"* and *"in vitro"* breeding techniques are not regulated by EU Directive 2001/18. The reader should note that the CJEU and Advocate General Szpunar disagreed with the Council of State's factual statements, in its 7 February 2020 opinion, about *"in vitro"* techniques being of recent development and usage (i.e., after the year 2001).

In summary, the CJEU opinions of 2018 and 2023 make the following distinctions for EU law and regulations. First, genetically modified plants and gene-edited plants are considered post-2001 breeding techniques that are subject to the EU Directive 2001/18. Second, classical chemical or radiation mutagenesis, whether accomplished *in vivo* or *in vitro*, are considered conventional pre-2001 breeding techniques and, therefore, not subject to EU Directive 2001–18.

The impact of the two *Confédération paysanne* cases is to do exactly what AG Bobek foresaw in his 2018 Advisory Opinion. The EU regulatory regime related to modern plant breeding is frozen in time (pre-2001 versus post-2001) and prohibits genetically modified plants and gene-edited plants from being in commercial use in Europe unless plant breeders gain authorization through the stringent requirement of Directive 2001/18. In reality, plant breeders have rarely even tried to gain approval. Except for one transgenic crop, approved under EU law in 1998 prior to Directive 2001/18, there are no genetically modified or gene-edited crops grown in European agriculture. Field testing is basically non-existent in Europe. When plant breeders do attempt field tests, activist vandals destroy the test plots (Negri, 2024).

EU Directive 2001/18, the focus of the judicial opinions explained above, relates to the release of crops into the environment (i.e., farmers' fields in the EU). A separate and distinct Regulation (EU) No. 1829/2003 governs approval for food and feed uses of products consisting, containing, or derived from genetically modified organisms, regardless of whether they have been imported or not. Under the authority of Regulation (EU) No. 1829/2003, the EU Commission has authorized more than seventy foods and feeds from genetically engineered and gene-edited crops for the EU consumer markets. European animal agriculture uses significant quantities of GMO feedstuffs and would not be able to satisfy consumer demand for animal products without these GMO feedstuffs [USDA GAIN EU, 2023, *passim*]. By contrast, European food companies and grocers have been very reluctant to sell (as a practical matter, almost banned) foodstuffs containing ingredients from genetically modified or gene-edited crops from their inventory and grocery shelves.

The way forward for modern (post-2001) agricultural biotechnology is through legislative and regulatory action. In July 2023, the European Commission (EC) presented a proposal to the Council of the EU (the member states) to amend EU laws and regulations related to crops developed by the use of NGTs. In March 2025, the Council of Europe reached agreement on a common position related to the July 2023 EC proposal. By agreeing to a common position, trilateral negotiations between the Council, the EC, and the EU Parliament can begin about what amendments specifically will be made, if any, to the EU laws and regulations related to gene-edited plants. As of May 2025, this trilateral negotiation has just begun and is expected to take approximately 2 years (Morrison Forester, 2025).

In the political and cultural climate that presently exists in Europe, it is unlikely that agricultural biotechnology will be accepted any time soon. While the EC and the Council have proposed changes in the EU legal regime related to agricultural biotechnology, even these recent proposals face significant opposition. The European deadlock about agricultural biotechnology apparently has no foreseeable end (Brookes and Smyth, 2024).

Kenya

On 8 November 2012, the Cabinet of the Republic of Kenya directed the Minister of Health to use Kenyan health and sanitation laws to prohibit the importation of food and feed from genetically modified crops and to prohibit the cultivation within Kenya of genetically modified crops. This Cabinet decision controlled until 3 October 2022 when the Cabinet of the Republic of Kenya lifted the 2012 prohibition. In 2022, the Cabinet allowed the National Biosafety Authority to use and execute Kenyan laws and regulations, that had been adopted in earlier years, to authorize importation and cultivation of genetically modified crops, food, and feed. Due to this 2022 Cabinet order, under previous decisions of the National Biosafety Authority, Kenyans could import and grow genetically modified white maize (corn) [Kenya Peasants League, 2025, ¶¶ 1& 5].

Soon thereafter, on 16 January 2023, the Law Society of Kenya (Law Society) filed a petition with the Environment and Land Court (E&L Court) at Nairobi. In the petition, the Law Society asked for a declaration by the E&L Court that the Attorney General (that is, the Government of Kenya [GOK]) had violated the rights of the Law

Society and the Kenyan public to a clean and healthy environment. The Law Society also asked the E&L Court to mandate that the GOK be prohibited from allowing further cultivation, importation and exportation of genetically engineered maize and other requested relief. By this lawsuit, the Law Society was challenging the Cabinet's 2022 decree lifting the 2012 ban on genetically modified crops, food, and feed. The case name is: *Law Society of Kenya v. Attorney General* [Law Society, 2023, ¶ 1 Judgment.]

After a thorough and extensive presentation of the submissions and legal arguments of the Law Society and the Attorney General and the relevant legal authorities domestically and internationally, the Justice of the E&L Court gave his analysis and determinations. To understand the decision, the best approach is to quote various paragraphs from the E&L Court judgment.

On 12 October 2023, the E&L Justice wrote,

> "[298] What the court is called upon to determine is the effectiveness of the existing laws and regulations in as far as identifying, mitigating and addressing potential risks taking into account key environmental principles and concerns, and in particular the precautionary principle in sustainable development.
>
> ". . .
>
> "[330] It is not clear to this court why all these approvals [prior GOK approvals of GMOs for cultivation and import as food/feed] have not been challenged by the Petitioner [Law Society] if indeed there is a concern that GM foods pose a serious risk to the environment and human health.
>
> "[331] In conclusion, it is the finding of this court that the Petitioner has not challenged the constitutionality of the laws governing GMOs, both international and domestic. The regulatory barriers that govern importation and cultivation of GMOs remain in force, and the same are presumed to be constitutional until the contrary is proven.
>
> ". . .
>
> "[337] The existing legal and institutional framework has been set up for the rigorous evaluation of GM organisms and GM foods relative to both human health and the environment. The evidence before the court shows that the National Biosafety Authority and other Agencies have the capacity in the identification of foods that should be subject to risk assessment and recommend appropriate approaches to safety assessment.
>
> ". . .
>
> "[339] Let me end by stating that as a country, we need to trust the institutions that we have in place, and call them to order in the event they breach the law. The *Biosafety Act* stipulates that the National Biosafety Authority should work in close collaboration with the Department of Public Health, which safeguards the health of consumers through food safety and quality control, surveillance, prevention and control of food borne diseases.
>
> ". . .
>
> "[342] With all these institutions, we should be confident that our health and environment is in good hands. It cannot be true they have all conspired to expose the rest of the population to the calamities alluded to in the Petition.
>
> "[343] This court has not been shown any evidence to show that the Respondents [GOK] and the institutions named in the preceding paragraphs have breached the laws, regulations and guidelines pertaining to GM food, and in particular the approval of the release in the environment, cultivation, importation and exportation of Bt maize.
>
> "[344] For those reasons, the petition dated 16 January 2023 is dismissed. . ." [Law Society, 2023, ¶¶ of Judgment given in the text quotations.]

Opponents of agricultural biotechnology did not passively accept the Judgment of the E&L Court. The opponents previously had filed three additional petitions (dated 18 September 2015, 13 October 2022, and 22 November 2022) against the GOK for authorizing the cultivation, importation and exportation of genetically modified crops. For these additional petitions, the opponents filed in the High Court of Constitutional and Human Rights at Nairobi. These petitions gave rise to a second case, as the High Court consolidated the three petitions into one proceeding: *Mwangi v. Attorney General* (2024) [Mwangi, 2024, ¶¶ 3–5].

On 7 November 2024, the High Court of Constitutional and Human Rights (High Court C&HR) rendered a ruling in this second case that never reached the substantive legal arguments and issues. Rather, the High Court C&HR immediately took notice that a court of equal status (the E&L Court) had already rendered a judgment on what appeared to be the same substantive legal arguments and issues. Thus, the High Court C&HR instructed Mwangi and the Attorney General to develop an analysis of whether the E&L Court decision was final and binding on the High Court C&HR so as to preclude continuing litigation and re-litigation. In legal terms, the High Court C&HR wanted to know about *res judicata* and *collateral estoppel*, which are legal terms that relate to the ability of parties in a dispute to relitigate decisions. [Black's Law Dictionary].

The High Court C&HR decision can best be understood by reading several paragraphs of its opinion;

> "[72] It is manifest that the Environment and Land Court judgment largely focused on the validity of the (GOK) decision to lift the ban of GMO foods in Kenya. That was the substratum of the case before the Environment and Land Court which considered the implication of lifting the ban on GMO foods in relation to the importation and exportation of Bt maize.
>
> "[73] In arriving at its decision ELC made findings on a host of issues that were raised in the case. A significant determination that was made was on the safety of GMOs. The Court made a finding that the laws and regulations in place both nationally and internationally are proper and were made in a manner that

> guards against violation of fundamental rights such as protection of the right to a clean and healthy environment. The Court also noted that the laws were in harmony with the precautionary principle as interpreted by the Courts.
>
> "[74] Additionally, it was observed that the (Law Society) had failed to challenge the constitutionality of the laws that govern GMOs and hence those laws enjoy the presumption of constitutionality until proven otherwise. . . .
>
> ". . .
>
> "[81] In view of the foregoing reasons, it is the finding of this Court that the current consolidated Petition is *res judicata*. The Court would be regurgitating the same issues that were exhaustively dealt with by the ELC Court if it were to insist on hearing the consolidated Petition. I hereby strike out the same with no order as to costs." [Mwangi, 2024, ¶¶ of Ruling given in the text quotations.]

The Kenya Peasants League (KPL) appealed the decision of the High Court C&HR to the Kenya Court of Appeal. On 7 March 2025, the Court of Appeal ruled that the KPL had the legal right to appeal the High Court C&HR decision. The Court of Appeal made it clear that this 2025 appeal was only on the issue of whether the High Court C&HR had correctly ruled about the doctrine of *res judicata*. In other words, the Court of Appeal, by allowing the appeal, was only addressing the procedural issue about relitigation. The Court of Appeal made it clear that the underlying substantive issues, relating to constitutional issues about a clean and healthy environment, are not part of this 2025 appeal. The Court of Appeal docketed the hearing on the 2025 relitigation appeal for the second term of 2025. In Kenya, the second court term begins in late April 2025 [Kenya Peasants League, 2025, ¶¶ 50–53].

By these three decisions (Law Society, 2023; Mwangi, 2024; Kenya Peasants League, 2025), the alternative paths forward for Kenyan litigation are as follows:

If the Kenyan courts rule, in the latter half of 2025, for the KPL (i.e., that the KPL can relitigate various legal issues), the Kenyan Courts will then schedule appropriate procedures for evidence presentation, written briefs, appeal hearings, and oral arguments on the substantive underlying constitutional issues. If allowed, the precise timeline for this potential new KPL substantive litigation cannot be known as of May 2025. But most likely, this new substantive appeal could not be resolved prior to court terms in 2026. If the Kenyan courts were to allow a substantive constitutional challenge about agricultural biotechnology, and if the Kenyan courts were to rule in favor of KPL's constitutional challenge, then ultimately Kenyan courts would have reversed the decision of the E&L Court of 12 October 2023. In that event, due to litigation and judicial rulings, Kenya would then have a constitutional ban on agricultural biotechnology.

If the Kenyan courts rule against the KPL and uphold the ruling of the High Court C&HR, the Kenyan courts will have upheld the action of the Kenyan Government in October 2022 to lift a ban on genetically modified crops and foods. If the KPL 2025 relitigation appeal is denied, Kenya would have approved Bt cotton and Bt maize for cultivation and approved imports of genetically modified foods in accordance with the E&L Court decision. As the E&L Court stated, paraphrasing, as long as plant breeders comply with the regulatory structures (regulatory barriers) existing in Kenya to gain approval for genetically modified (and by implication gene-edited) crops and foods, Kenyan agriculture would be ready to begin using crops and foods created by modern plant breeding techniques.

But which path Kenya actually follows cannot be known in May 2025 because the chosen path depends on the outcome of the KPL 2025 relitigation appeal and potential future constitutional litigation likely extending into the year 2026. Hence, any prediction that Kenya appears to be on the verge of becoming a nation that consumes and grows genetically modified and gene-edited foods and crops has turned out, because of on-going litigation, to be premature [USDA GAIN Kenya, 2024, *passim*].

Ghana

In January 2015, the Government of Ghana, through the National Biosafety Committee and the Ministry of Food and Agriculture, took steps to authorize the commercial release of Bt cowpea. In response to these steps, on 8 February 2015, Food Sovereignty of Ghana (FSG) (and others) filed a lawsuit to challenge the introduction of genetically modified crops into the nation. In this February 2015 legal challenge, FSG sought an injunction against the government. [Black's Law Dictionary] In October 2015, the Accra High Court dismissed FSG's application for an injunction (Ghana New Agency, 2015).

In response to this procedural loss, FSG filed a new lawsuit, on 23 November 2017, against the National Biosafety Committee and other governmental entities. FSG argued that the plans to commercialize genetically modified crops into Ghana had not followed authorizing legislation nor followed required administrative procedures (Gakpo, 2017). After several preliminary legal rulings, this 2017 lawsuit gave rise to the 24 May 2024 decision of the High Court of Human Rights (HCHR) in Accra: *Food Sovereignty of Ghana v. National Biosafety Authority* (NBA, 2024).

On 24 May 2024, the HCHR issued its opinion in the 9-year long litigation. In the opinion, the presiding Justice of the HCHR described the lawsuit as a "red herring" that had failed to provide evidence that undermined the Ghanaian regulatory system. The HCHR emphasized that the NBA and other agencies had conducted an extensive scientific and socio-economic review of the application for environmental release of genetically modified Bt cowpea. The HCHR ruled that the NBA and other agencies had complied with the Ghanaian Biosafety Act of 2011 and with international best practices. However, the Justice also directed the NBA to provide further public education and to finalize regulations related to labeling of genetically modified products before any commercial release of approved crops into Ghanaian farmers' fields (Biotech Updates, 2024; NBA, 2024).

The HCHR decision upheld the NBA's 2022 approval of the environmental release of Bt cowpea. While the HCHR 2024 decision indicated that Ghanaian governmental agencies have additional tasks to complete before the actual release of genetically modified crops, Ghana appears to be positioned to allow its farmers to grow genetically modified crops beginning in 2025. The author also thinks

that the HCHR judgment impliedly affirmed the NBA's decision, in April 2024, allowing the import of genetically modified maize and genetically modified soybean for food, feed and processing. Ghana imports significant amounts of foodstuffs and feedstuffs that contain processed genetically modified ingredients. Moreover, in 2023, the NBA adopted guidelines on gene-edited crops to provide clarity about which gene-edited crops are covered by the Biosafety Act of 2011 and which are not [USDA GAIN Ghana, 2024, *passim*.].

Taking into account the HCHR's judgment and the NBA actions and decisions related to genetically modified crops and gene-edited crops, Ghana is moving forward to use modern plant breeding techniques in agriculture.

The Philippines

MASIPAG, Greenpeace and other Filipino environmental organizations and individuals have been contesting governmental actions related to genetically modified crops in the Philippines since 2002. In 2002, the Philippines agricultural research universities and institutes began field testing Bt corn. In 2005, the Philippines government approved the commercial release of Bt. corn. Bt corn has been grown ever since in the Philippines. In 2012, as the Philippines government moved to approve field testing of Bt eggplant (talong in Tagalog), MASIPAG, Greenpeace, and their supporting complainants challenged the legality of these Bt eggplant field trials (Ocampo, 2013). In 2017, MASIPAG and Greenpeace similarly challenged applications for field trials and direct use of Golden Rice.

After many legal proceedings from 2012 through 2023, the Supreme Court of the Philippines consolidated the challenges to Bt eggplant and Golden Rice into a legal proceeding for the issuance of a Writ of Kalikasan. (In Tagalog, the word kalikasan means "nature" – Writ of Nature.) [Writ of Kalikasan defined] Therefore, a Writ of Kalikasan offers petitioners a legal procedure to seek legal protection for the environment.

On 18 April 2023, the Supreme Court of the Philippines, ordered the Court of Appeals Fourth Division in Manila to hear and resolve the consolidated lawsuit. [MASIPAG April 2024, pp. 2–7] Accordingly, the Court of Appeals issued two opinions in 2024 in this consolidated matter: *Magsasaka at Siyentipiko Para SA Pag-Unlad Agrikultura (MASIPAG) v. Secretary of Agriculture*, [MASIPAG April 2024] and *Magsasaka at Siyentipiko Para SA Pag-Unlad Agrikultura (MASIPAG) v. Secretary of Agriculture*, [MASIPAG August 2024]. MASIPAG August 2024 is an Amended Decision to the April 2024 decision.

The ruling of the Court of Appeals in August 2024 can best be stated by quoting from the decision itself.

> p. 18 "The compelling interest and paramount importance of the instant case far outweigh technicalities that impede the cause of justice. If the stringent application thereof [procedural rules] would hinder rather than serve the demands of substantial justice, the former must yield to the latter. . ."

> p. 19 "The precautionary principle applies; the grant of the privilege of the writs of kalikasan and continuing mandamus [supervision] [in this Court's April 2024 decision] was proper. . . .

> p. 20 There is no evidence that would show that GMOs do not pose greater risks than their conventional counterparts, especially considering that the [Secretary of Agriculture and other] regulators fell short of conducting the risk management and monitoring mechanisms required under the Joint Department Circulars (JDCs). Clearly, the determination of such risks can only be done if there are proper monitoring mechanisms implemented. Unfortunately, it was revealed during trial that the [Secretary of Agriculture and other] regulators have no such measures in place.

> p. 20 All things considered the balancing of evidence adduced by the parties calls for a conclusion that the constitutional right of the people to a balanced and healthful ecology must be given the benefit of the doubt." [MASIPAG August 2024, pages given in text quotations.]

Flowing from these rulings, the Court of Appeals ordered the Secretary of Agriculture and other respondent regulators to revoke the permits for the commercial release of Bt eggplant and Golden Rice, cease and desist from activities related to Bt eggplant and Golden Rice and (quoting):

> p. 32 "Item 6. Enjoining the commercial propagation and/or conduct of activities relating to Golden Rice and Bt Eggplant until such time that the concerned respondent government agencies submit proof of safety and compliance with all legal requirements; and

> "Item 7. Ordering concerned respondents government agencies to perform their mandate under the applicable JDC, by submitting to this Court the concrete mechanisms adopted to monitor all activities conducted under the JDCs, and all measures taken to strengthen the risk assessment procedure set forth in JDC No. 1–2021 in accordance with the ruling in this case." [MASIPAG August 2024, pages given in text quotations.]

In the August 2024 amended decision, the Court of Appeals deleted Item 8 of its April 2024 Order. Item 8, from the April 2024 Order, had read as follows:

> "Item 8. Enjoining any application for contained use, field testing, direct use as food or feed, or processing, commercial propagation, and importation of genetically modified organisms until compliance with (Item 7) [identical in both the April 2024 Order and the August 2024 order] above is established." [MASIPAG April 2024, p. 142].

As written in April 2024, the Court by Item 8 had seemingly completely banned genetically modified crops and products, including imports, from the Philippines. But in the year 2024, the Philippines imported significant amounts of genetically modified food and feed. Moreover, the Philippines had been growing Bt maize for many years. Upon reconsideration of its April 2024 Order, the Court of Appeals in August 2024 ruled that other genetically modified crops and imports were not part of the MASIPAG case against Bt eggplant and Golden Rice. Hence, in August 2024, the Court Appeals decided that these other

genetically modified crops and imports had not received an opportunity for being heard in litigation. Consequently, the Court of Appeals August 2024 Order deleted Item 8 of the April 2024 Order on the concern that Item 8 violated a fundamental right to due process. [MASIPAG August 2024, p. 31.]

The Philippine regulatory agencies have granted commercial release for four genetically modified crops: maize (2002), Golden Rice (2021), eggplant (2022), and cotton (2023). Filipino farmers planted 709,000 ha (1,751,939 acres) of genetically modified maize in the most recent planting year. The Philippines imports 60%–70% of its animal feed in the form of genetically modified maize or soybean. The Philippine regulatory agencies have also granted four certificates of non-genetically modified status to bananas and tomatoes created through gene-editing techniques. Filipino regulatory agencies are using "certificates of non-genetically modified status" to distinguish some gene edited crops from genetically modified crops [USDA GAIN Philippines, 2024, *passim*.].

The present status of this wide-spread use of genetically modified organisms in the Philippines is apparently the following:

The Court of Appeals ruling of August 2024 only applies to Golden Rice and Bt eggplant. As of May 2025, this Court of Appeals August 2024 ruling is apparently stayed (in abeyance) as the Philippine Rice Research Institute (PhilRice) appeals to the Supreme Court of the Philippines to reverse or modify the Court of Appeals decision (PhilRice, 2024). If the Supreme Court rules for PhilRice, Filipino farmers will have access to Golden Rice, Bt eggplant, Bt/HT maize, and Bt/HT cotton. If the Supreme Court rules against PhilRice, MASIPAG has successfully blocked Golden Rice and Bt Eggplant. Furthermore, MASIPAG would have a precedential (binding) decision upon which to rely to block genetically modified maize and cotton. MASIPAG would only need to file another lawsuit seeking a Writ of Kalikasan for these two additional crops.

As for imported genetically modified feedstuffs, the Court of Appeals August 2024 ruling allows continued importation, but MASIPAG threatens to file legal challenges against these imports [MASIPAG, 2024, pp. 2–3].

Concerning gene-edited crops, as contrasted with the more traditional genetically modified crops mentioned previously, the Court of Appeals decisions did not address these breeding techniques. The Court of Appeals decisions said nothing about the granting of certification of non-genetically modified status to bananas and tomatoes. MASIPAG likely opposes gene-edited crops as strongly as it opposes genetically modified crops and, therefore, seems likely to take legal action against gene-edited crops also. Thus, the ultimate legal status of gene-edited crops in the Philippine courts is an unknown, awaiting further legal proceedings and developments.

With litigation still in the Philippine Supreme Court, as of May 2025, the future of agricultural biotechnology is at a historical tipping point. If the Supreme Court rules for the Secretary of Agriculture, the Philippines could be an Asian leader in the use of biotechnology in agriculture. If the Supreme Court rules for MASIPAG, Filipino agriculture will be blocked from using agricultural biotechnology–and blocked for an indeterminate time into the future. Until this litigation is resolved, agriculture in the Philippines faces great uncertainty about the use or non-use of agricultural biotechnology.

South Africa

In July of 2014, Monsanto Corporation applied for a permit for the general release of a drought-tolerant genetically modified maize (MON 87460). In 2015, the African Center for Biodiversity (ACB) opposed this application, thereby initiating litigation that lasted 9 years [ACB, 2023, ¶¶5–6]. The litigation resulted in two published opinions in the courts of South Africa: *African Centre for Biodiversity NPC against the Minister of Agriculture Forestry and Fisheries* (ACB, 2023), and *African Centre for Biodiversity NPC v. Minister of Agriculture, Forestry and Fisheries and others* (ACB, 2024).

In ACB 2023, the High Court denied the petition of the ACB and ruled as valid the general release of MON 87460. More specifically, the High Court judge wrote:

> "[48] The Appeals Board considered everything that was before the EC (Executive Council for Genetically Modified Organisms) and had available the submissions of ACB, including the reports of their experts. The Appeal Board considered all of this and concluded that the permit should be granted. There is no evidence that the decision was either irrational or unreasonable. Nor was there any credible evidence that either the EC or the Appeals Board did not apply their minds to the information before them. Despite the allegations of bias and/or influence by third parties, no objective evidence was provided to prove that, or any unlawful delegation of power." [ACB, 2023, ¶ cited in the text quotation.]

ACB appealed this High Court ruling to the Supreme Court of South Africa. The Supreme Court of South African set aside the High Court ruling and issued a new order. The Supreme Court ruled that the permit granted for MON 87460 was invalid and referred the Monsanto (now Bayer) application back to the regulatory agencies of South Africa for reconsideration [ACB, 2024, Order at ¶ 25(3)].

In ruling for the ACB, the Supreme Court wrote:

> "[24] The high court conflated the obligation arising from section 5(1)(a) of the Act (Genetically Modified Organisms Act 15 of 1997) with the applicability of the precautionary principle, finding that an environmental impact study would only be required in the event of the precautionary principle being triggered. First, as addressed above, the precautionary principle was triggered and ought to have been applied. Second, whether the Executive Council, as a matter of fact, complied with section 5(1)(a) by considering the necessity of an environmental impact study to ascertain the impact on the environment of the proposed general release of MON 87460 was a separate and distinct inquiry from whether the precautionary principle was triggered and should have been applied. . . . The ineluctable conclusion is that the Executive Council failed to comply with a mandatory statutory prescript contained in section 5(1)(a). This means that the Executive Council's decision cannot stand. Nor, for that matter, it must follow,

> can the decisions by the Appeal Board and the Minister." [ACB, 2024, ¶ cited in the text quotation.]

South Africa has been growing genetically modified crops since the late 1990s. South Africa has approved thirty-three genetically modified traits for general release for cultivation [USDA GAIN, 2024, Table A1]. Since 2018, South Africa has approved field trials for an additional thirty-five genetically modified crops. [USDA GAIN, Table A2]. South African farmers widely plant three genetically modified crops: maize (corn), soybean, and cotton. As an example, for maize, South African farmers have used genetically modified varieties on more than 80% of planted hectares for the past seven crop years. [USDA GAIN, Table 1] South Africa has approved 108 genetically modified traits for import for food and feed use. [USDA GAIN, Table A3] South Africa is a exporter of genetically modified maize and soybeans [USDA GAIN, Table 2 &3]. South African agricultural research institutions are active in using modern biotechnology for crop breeding and improvement. [USDA GAIN, pp. 4–5]. Up until 2025, South Africa has been a world-wide leader in the adoption of genetically modified crops for cultivation, food, feed, import and export.

Although the Supreme Court of South Africa ACB 2024 decision is only about the general release of one genetically modified maize trait (MON 87640), the Supreme Court decision mandating both a distinct environmental impact statement and the application of the precautionary principle appears to apply to all genetically modified crops, field trials, foodstuffs and feedstuffs. Moreover, South African authorities ruled in August 2023 that new breeding techniques (for example, gene-editing techniques such as CRISPR, ZFN, and TALENS) will be regulated in the same manner as genetically modified organisms. [USDA GAIN, pp. 23–24] Thus, the Supreme Court ACB 2024 decision apparently will apply also to gene-edited crops, field trials, foodstuffs and feedstuffs.

South African agriculture is facing a very uncertain future regarding agricultural biotechnology. South Africa may change from being a world-leader in modern agricultural biotechnology to being a nation that, as a practical matter, bans it. South Africa may go from reaping the benefits of agricultural biotechnology to a nation that has chosen, through judicial decision, to abandon these benefits and to forego these benefits in the future (Cooper, 2022; Gbashi et al., 2021; Ala-Kokko et al., 2021; Gouse et al., 2016).

United States

The United States Department of Agriculture, Animal and Plant Health Inspection Service (APHIS) first issued regulations for genetically modified plants in 1987. The 1987 regulations focused on risks from plant pests being used to genetically modify plants–most prominently *Agrobacterium tumefaciens* (a bacterium used to physically transfer a gene into a cell of the plant being transformed) and the use of promoter sequences from a plant virus (e.g., cauliflower mosaic virus). By the early years of 2000, plant breeders were able to genetically modify plants without the use of plant pests, either by direct gene transfer using "gene guns," or by the removal of plant pest genes from the finished modified plant (null segregant plants), or through gene-edited techniques such as ZFN and TALENS. APHIS responded to non-pest modified plants by issuing letters to plant breeders, when plant breeders inquired, informing them that APHIS did not consider these non-pest modified plants to be within the APHIS regulations (Entine et al., 2021).

In a related development, the US government enacted the Plant Protection Act (PPA 2000), The PPA 2000 consolidated ten federal statutes dealing with plant pests, noxious weeds, invasive species and other potential threats to American agriculture. The PPA 2000 redefined noxious weed concerns as a consideration for APHIS in its regulatory mandate (APHIS, 2002).

Beginning in 2004, APHIS undertook a rule-making process to revise the US regulations governing plant biotechnology, taking into account PPA 2000, several executive orders, and other studies related to agricultural biotechnology regulation (Entine et al., 2021). APHIS completed this revision in 2020 with the adoption of a regulation (called the SECURE rule) that put more focus on the specific trait in the biotech plant, than upon the process by which the plant was created. [NFFC 2024, pp. 3–5]. Led by the National Family Farm Coalition and the Center for Food Safety, various opponents of agricultural biotechnology sued in the U.S. District Court for the Northern District of California asking for relief declaring the APHIS 2020 regulation invalid. Two published opinions resulted from this litigation: *National Family Farm Coalition v. Vilsack* (NFFC, 2024), and *National Family Farm Coalition v. Vilsack*, (NFFC, 2025).

The District Court Judge ruled in favor of the NFFC and its co-plaintiffs on two grounds. First, the District Court determined that APHIS had not adequately explained why it had not incorporated noxious weed considerations into its 2020 regulation [NFFC, 2024, p. 7–9]. Second, the District Court concluded that APHIS had not adequately explained why it exempted plants created by biotechnology from the 2020 regulation when these plants were equivalent to conventionally bred plants, even though conventionally bred plants can create, at times, plant pest and noxious week risks [NFFC, 2024, pp. 9–10]. The District Court vacated the 2020 regulation and remanded to APHIS for reconsideration of appropriate plant biotechnology regulations in a manner consistent with its 2024 opinion [NFFC, 2024, p. 2].

The District Court then addressed the appropriate remedy and wrote:

> "...the Court is mindful that the rule took effect in 2020 and that this area of our national agricultural economy is rapidly developing. . . . at least 99 new GE plants have been exempted . . . retroactive vacatur 'seems an invitation to chaos.'. . . [Black's Law Dictionary].

> "Consequently, the Court concludes that the remedy that best balances the law and that which 'equity demands' . . . is vacatur of the final rule as of the date of this order . . . this form of vacatur suffices to return the industry and GE-crop regulations to the *status quo ante*." [NFFC, 2024, p. 13]

By vacating the rule "as of the date of this order," the District Court was allowing previous approvals by APHIS under the 2020 SECURE regulation to remain valid, but also was telling APHIS that the 2020 SECURE regulation could no longer be used in future regulatory decisions.

As for the January 2025 opinion, the District Court in December 2024 told the parties to return to the Court to litigate unresolved issues. When the parties returned, the District Court decided that the unresolved issues were legally moot–i.e., no longer before the Court–because the December 2024 vacatur had settled all the issues. [NFCC, 2025, pp. 1–2]. In April 2025, the US dismissed its appeal from the District Court rulings. Hence, as of May 2025, APHIS regulates under the regulations written prior to 2020.

United States agricultural researchers extensively utilize biotechnology breeding techniques. United Sates farmers plant millions of hectares of genetically modified and gene-edited crops every crop year. Companies use genetically modified and gene-edited crops and ingredients from those crops in many foodstuffs and feedstuffs. American grocery shoppers consume biotechnology foodstuffs in great quantities. Animal agriculture in the US relies heavily upon genetically modified and gene-edited feedstuffs. The United States is the world's leader in the adoption of biotechnology in agriculture.

The District Court opinions mean that APHIS has returned to a plant biotechnology rule that focused heavily upon the process by which plants were created. The APHIS regulations prior to 2020 used the trigger of genetic modification to assert regulatory control over plant biotechnology. How significant this return to "process" over "product" in agricultural biotechnology will be depends upon how APHIS responds. Even under the pre-2020 regulatory regime, US agriculture widely used genetically modified breeding techniques and crops. Thus, returning to the pre-2020 regulations does not mean a turn away from agricultural biotechnology for American agriculture. What the return to the pre-2020 regulations might mean is that the pace of the adoption of agricultural biotechnology may be slowed temporarily or may be slowed for a significant period of time into the future (Kershen and Miller, 2025).

Part Two: commentary and critique

After reading the summaries of the judicial opinions of the seven jurisdictions, a reader could conclude that the opinions simply express the laws and regulations of that jurisdiction. While the reader might wish that the judicial opinions had been decided differently, the reader could think that the judges, who wrote those opinions, have done their best to understand and to interpret the facts and the laws in each particular legal matter. While this view of these opinions has validity, this benign acceptance of these opinions overlooks that the judges in each legal matter made choices about the facts and laws. The judges made choices about which legal interpretations to adopt as the rulings and orders of the court. The judges chose between competing, plausible interpretations of the laws and regulations of these seven jurisdictions.

The judges did not simply discover the facts and laws; the judges choose the facts and laws to reach their judicial conclusions. These judicial opinions reflect choices by human actors (judges). On the choices these judges made, this author can provide commentary and express critiques that are more than the personal fulminations of a pro-agricultural biotechnology author. By carefully reading the facts, laws, and interpretations of these judicial opinions, the author can highlight common themes. By carefully reading the facts, laws, and interpretations in these judicial opinions, the author can identify critiques based on the internal evidence of the lawsuits themselves. By so doing, the author's commentary and critiques present an analysis of these legal matters that provides an understanding that the judges could have chosen differently. And, the author contends, the judges could have chosen better legal paths forward for agricultural biotechnology and for society as a whole.

Agricultural science and innovation

The judicial opinions of New Zealand and the European Union (EU) are remarkably similar. In both opinions, the judges choose to subject newer, innovative gene-editing breeding techniques to the same legal and regulatory regime as previous genetic-engineering techniques. By so doing, the judges greatly slowed gene-editing from being used in their agricultural sectors. As a consequence of these judicial opinions, neither New Zealand or the EU have allowed gene-edited field trials or gene-edited crops to enter into the mainstream of agricultural research and farmers' fields. Moreover, as New Zealand and the European Union have been very reluctant to authorize the cultivation of crops from previous genetic-engineering techniques (none in New Zealand and one in the EU), by subjecting gene-edited crops to the same regulatory system as previous genetic-engineering techniques, the judges have effectively precluded gene-edited crops from the fields of New Zealand and the EU.

In both instances, governmental authorities (in New Zealand, the EPA's Section 26 Committee; in the EU, Advocate General Bobek) had expressed and argued a clear determination that many gene-edited techniques, including those techniques factually at issue in the actual litigation, were equivalent to chemical mutagenesis. As both New Zealand HSNO 1996 and EU Directive 2001/18/EC expressly exempt chemical mutagenesis from the burdens and strictures of the regulatory regimes deployed against previous genetic engineering, equivalent gene-edited techniques would be an expansion or extension of chemical mutagenesis. Therefore, the equivalent gene-edited technique would not be new and novel--as the legislators had considered the previous, regulated genetic-engineering techniques. The judges in the New Zealand and EU lawsuits could have chosen, legitimately, to adopt this equivalence and, consequentially, this exemption for gene-edited breeding techniques. By refusing to choose this equivalence option, the judges showed reluctance and skepticism to science (modern molecular biology and modern plant breeding) and to agricultural innovation (Monaco, 2024).

Similarly, in the recent judicial opinion (NFCC, 2024) in the United States, the judge could have ruled for USDA-APHIS. APHIS had spent 16 years developing a 2020 SECURE regulation focusing on the product of agricultural biotechnology, rather than focusing on the process used in agricultural biotechnology, as the pre-2020 regulations had done. By failing to understand or acknowledge the product versus process distinction, the judge disregarded scientific advances in molecular biology and agricultural innovation (McHughen, 2016).

The US judge showed a reluctant attitude toward more precise, better understood, more predictable techniques of plant breeding.

The US judge required APHIS to return to outmoded and scientifically unjustified process triggers. The judge expressed an inkling of understanding when the judge developed a case-made remedy that vacated the 2020 rule only prospectively, rather than retroactively, so as to protect numerous gene-edited plants APHIS has already approved under the 2020 SECURE regulation. But that specially designed remedy also indicates, impliedly, that the judge could have granted APHIS a period of time (e.g., 120 days) to explain more fully its decisions about the 2020 SECURE regulation. At the end of that period, the judge then could have decided if the APHIS 2020 rule accorded with transparency, reasonableness and considered rationality. Instead, the judge made a choice to endorse arguments by opponents of agricultural biotechnology that, in this author's opinion, are based on misunderstanding, misinformation and obscurantism about science and agriculture. The US judge fully disapproved the 2020 SECURE rule and sent the US regulatory system for agricultural biotechnology back to the past.

Regulatory agencies of agricultural biotechnology

Courts rightly should hold regulatory agencies accountable for their decisions. Courts are tasked properly with insuring that regulatory agencies comply with their enabling laws and regulations. However, courts should not undermine trust in regulatory agencies by endorsing claims by opponents of agricultural biotechnology that attack the integrity of regulatory agencies. As the pleadings and presentations from the litigation in the seven jurisdictions shows, opponents of agricultural biotechnology consistently impugn the integrity of regulatory agencies. [e.g., MASIPAG April 2024, pp. 32–72, Court summary of the evidence presented by the parties to the litigation.] Judges should be very careful that they do not adopt the opponents' attitude of impugning the integrity of regulatory agencies.

For example, in the litigation from South Africa, the Judge in the High Court (the lower trial court in South Africa) wrote as follows:

> "[2] . . . The crux of ACB's case is that the respective decision makers accepted the date included in Monsanto's application at face value and without ensuring that the necessary health and safety risk associated with MON 87460 had been properly and independently assessed" [ACB, 2023, ¶ cited in text quotation.]

The High Court pointed out that "It (MON 87460) has been approved for use in food, animal feed and environmental release in 17 countries, including the United States, the European Union, Korea and Japan." [ACB, 2023, ¶ 6] The High Court wrote:

> "[48] . . . Nor was there any credible evidence that either the EC or the Appeals Board did not apply their minds to the information before them. Despite the allegations of bias and/or influence by third parties, no objective evidence was provided to prove that, or any unlawful delegation of power." [ACB, 2023, ¶ cited in the text quotation.]

The High Court ruled in support of the regulatory agencies of South Africa which had granted the permit for general release.

The Supreme Court of South Africa expressed a different attitude and approach to the South African regulatory agencies than the High Court. The Supreme Court of South Africa summarized the ACB contentions as:

> "[10] The thrust of the appellant's (ACB] case is that the State respondents accepted at face value, the claims made by Monsanto and failed to independently an critically evaluate Monsanto's application to satisfy themselves that the health and safety risks associated with the general release of MON 87460 had been properly addressed. . . . Accordingly, so the contention proceeds: (a) The Executive Council accepted the data submitted by Monsanto without any consideration of the veracity, accuracy and completeness thereof; (b) the Appeal Board did not engage with the ground of appeal and the expert evidence, but simply rubber-stamped the decision made by the Executive Council; and, (c) the Minister further rubber-stamped the Appeal Board's decision by way of a confirmation letter that furnished no reasons at all." [ACB, 2024, ¶ cited in the text quotation.]

The Supreme Court reversed the High Court judgment and agreed with the ACB contentions. The Supreme Court vacated the South African regulatory agencies' approval for the general release of MON 87460.

The South African High Court and the South African Supreme Court exhibited strikingly different trust in the South African regulatory agencies governing agricultural biotechnology.

In contrast to the opinion of the Supreme Court of South Africa, the courts of Kenya and Ghana have been explicit in their trust for their nations' regulatory systems for agricultural biotechnology. As the Kenyan Judge of the Environment and Land Court wrote:

> "[339] Let me end by stating that as a country, we need to trust the institutions that we have in place, and call them to order in the event they breach the law. . . .
>
> ". . .
>
> "[342] With all these institutions, we should be confident that our health and environment is in good hands. It cannot be true that they have all conspired to expose the rest of the population to the calamities alluded to in the Petition." [Law Society, 2023, ¶¶ cited in text quotations.]

Regulatory agencies in countries around the world have considered applications related to agricultural biotechnology for 30 years. Regulatory agencies around the world have ruled favorably for the safety of agricultural biotechnology for human health and the environment. Borrowing language from the Kenyan Judge, "It cannot be true that they [the regulatory agencies of countries around the world] have all conspired to expose the rest of the population to the calamities alluded to in . . ." the pleadings and presentations of opponents of agricultural biotechnology. After 30 years of regulatory considerations, courts should show greater respect and trust for the regulatory agencies of agricultural biotechnology.

Precautionary principle

In the Philippines, the Supreme Court rules on the Writ of Kalikasan Rule 20 Precautionary Principle reads as follows:

> "Section 1. Applicability – When there is a lack of full scientific certainty in establishing a causal link between human activity and environmental effect, the court shall apply the precautionary principle in resolving the case before it. The constitutional right of the people to a balanced and healthful ecology shall be given the benefit of the doubt.

> "Section 2. Standards for application – In applying the precautionary principle, the following factors, among others, may be considered: (1) threats to human life or health; (2) inequity to present or future generations; or (3) prejudice to the environment without legal consideration of the environmental rights of those affected." [MASIPAG April 2024, pp. 79–80]

The Court of Appeals referred to Rule 20 of the Writ of Kalikasan in stating:

> "The precautionary principle bridges the gap in cases where scientific certainty in factual findings cannot be achieved. By applying the precautionary principle, the court may construe a set of facts as warranting either judicial action or inaction, to preserve and protect the environment. In effect, the precautionary principle shifts the burden of evidence of harm away from those likely to suffer damage and onto those desiring to change the *status quo*. Applying the precautionary principle to the rules of evidence will enable courts to tackle future environmental problems before ironclad scientific consensus emerges." [MASIPAG April 2024, p. 80]

In this author's opinion, using this understanding of the precautionary principle, the Court of Appeals thereby gave credence to MASIPAG and Greenpeace that an "ironclad scientific consensus" does not exist. As their opposition to agricultural biotechnology since 2002 manifests, MASIPAG and Greenpeace will never accept the overwhelming scientific evidence that genetically modified and gene-edited breeding techniques and crops present no new or different risks to human health or the environment than conventional breeding techniques and crops. It is worth recalling the words from a European Commission Report of 2010 stating:

> "The main conclusion to be drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research and involving more than 500 independent research groups, is that biotechnology, and in particular GMOs, are not *per se* more risk than, for example, conventional plant breeding technologies." (European Commission, 2010)

Thus, an overwhelming scientific consensus does exist of the risk-level (equivalent to conventional plant breeding) for genetic-modification as a technique. But the Court of Appeals, using its interpretation of the precautionary principle, did not consider this overwhelming scientific evidence to be "ironclad."

Moreover, the Court of Appeals, using its interpretation of the precautionary principle, reversed the burden of presenting evidence and the burden of proof. Thus, the Court freed MASIPAG and Greenpeace from presenting evidence of harm from genetically modified crops (and there is no trustworthy evidence of meaningful harm to human health or the environment) and placed all the burden on the regulatory agencies to prove safety affirmatively, positively. Despite a fifteen-page summary of the regulatory agencies evidence about the safety of genetically modified crops for humans and the environment, the Court of Appeals evaluated this evidence as not sufficient to satisfy its interpretation of the precautionary principle's demand for "ironclad scientific evidence." [MASIPAG April 2024, pp. 16–31].

In refusing to consider the body of research to date as constituting ironclad scientific evidence of safety, the Court of Appeals, in effect, has positioned the Philippine judiciary as the ultimate arbiter of governmental decisions regarding agricultural biotechnology.

In the South African litigation, the Supreme Court quoted Principle 15 of the 1992 Rio Declaration on Environment and Development which states:

> "The precautionary approach states that where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." [ACB, 2024, ¶ 12]

Relying on Principle 15 of the Rio Declaration, the Supreme Court held:

> "[18] The high court's rejection of the appellant's [ACB] reliance on the precautionary principle was based on its finding that the precautionary principle does not find direct application in the review proceedings. However, such an approach disregards the fundamental role that the precautionary principle plays in directing decision-makers in the exercise of their discretion. The current state of knowledge and uncertainty, the potential for serious or irreversible harm and the adoption of a cautious approach is clearly consistent with the subject-matter, scope and purpose of the [Biosafety] Act [of 1997]." [ACB, 2024, ¶ cited in text quotation.]

While the Supreme Court of South Africa quoted Principle 15 of the Rio Declaration, the Court passed over and did not quote other principles from the Rio Declaration. For example, Principle 1 which reads:

> "Human beings are at the centre of concerns for sustainable development. They are entitled to a healthy and productive life in harmony with nature." (United Nations, 1992)

Or, for example, Principle 5 which reads:

> "All States and all people shall cooperate in the essential task of eradicating poverty as an indispensable requirement for sustainable development, in order to decrease the disparities

> in standards of living and better meet the needs of the majority of the people of the world." (United Nations, 1992)

By only quoting Principle 15, the Supreme Court of South Africa made no attempt at considering or reconciling other Principles in the Rio Declaration that may cast a more favorable light upon the work and decisions of the South African agencies related to agricultural biotechnology.

By ruling that the precautionary principle of Principle 15 alone applied in the litigation, the Supreme Court of South Africa seemingly arrogated to itself vast powers over agricultural biotechnology. Like the Court of Appeals of the Philippines, the Supreme Court decision in ACB 2024 apparently positions the judiciary to be the ultimate arbiter of governmental decisions regarding agricultural biotechnology.

Philippine and South African courts have disregarded 30 years of experience with agricultural biotechnology in which not a single instance of serious or irreversible damage exists to either human health or the environment. The courts disregarded this 30-year experience both world-wide and in their own nations. Moreover, the courts did not acknowledge the considerable benefits for human health, the environment, and the agricultural sector that agricultural biotechnology offers. The regulatory agencies of the Philippines and South Africa had offered this evidence of lack of harm and of benefits in the voluminous information comprising the litigation record. Rather, the courts chose to adopt the perspective of MASIPAG, Greenpeace, and ACB that speculative hazards should be given preference to lived experience and proven benefits. By so doing, the courts did not allow the precautionary principle to be a principle of common sense. Rather, the courts allowed opponents of agricultural biotechnology to use the precautionary principle as a trump card to block biotechnology from the agricultural sector. Under the circumstances of these cases, this is an abuse of the precautionary principle [Commission Staff, 2021, passim; Purnhagen and Wesseler, 2025, passim; Tagliabue, 2016, passim].

Value choices

In these legal proceedings, the opponents of agricultural biotechnology exhibit cynicism tied to their implacable opposition. From this author's perspective, their cynicism is unmoored from facts, science, truth, and morality. Several examples from the litigation provide evidence of this cynicism.

In the litigation in Kenya, the petitioners (opponents of agricultural biotechnology) attacked the Executive Order of October 2022 lifting a ban on cultivation of agricultural biotechnology crops. The ban originated with a prior Executive Order issued on 12 November 2012 that had asserted concerns for human health as justification for the summary action. The Executive Order of 2012 based its concerns upon a 2012 published study by Séralini, E. and others [Law Society, 2023, ¶¶ 31–36 of Judgment]. Within days of the publication of the Séralini study, many scientists criticized the study for its methodology, its data interpretation, and its conclusions. By September and October of 2012, the controversy about the Séralini study was widely reported (Independent Science News, 2012; Mole, 2012). Thus, prior to the Executive Order 2012 in November 2012, the Kenyan Executive knew or should have known of the controversy about the Séralini study. As time passed, many scientists thoroughly refuted the Séralini study (FCT March, 2013; Arjó et al., 2013; Coumoul et al., 2018; Admin, 2018). The publisher retracted the study (Elsevier, 2013). In 2012, the Kenyan Executive summarily entered the 2012 Order without trusting the Kenyan regulatory agencies carefully to consider and assess the implications of the Séralini study for the regulation of agricultural biotechnology in Kenya. Rather, the Executive Order 2012 hobbled the Kenyan regulatory agencies making them relatively inactive for 10 years, until the Executive Order 2022, despite the valid criticisms and retraction of the Séralini study.

In the *Law Society* litigation, the petitioners opposed to agricultural biotechnology alleged that the Executive lifting of the ban in October 2022 was done illegally because it was done in a summary manner. The High Court E&L Judge rejected this allegation and remarked:

> "[250] As to whether there was public participation before the Cabinet Dispatch of October 2022, I have not been shown any law or authority that requires the Cabinet to engage the public before arriving at its decisions. In any event, there was no public participation before the ban of GMOs was imposed by the Cabinet in 2012." [Law Society, 2023, ¶ cited in the text quotation.]

As the quotation from the opinion of the High Court E&L clearly implies, the petitioners against the Executive Order 2022 were not opposed to summary action, but only summary action that did not align with their opposition to agricultural biotechnology and their opposition to a robustly functioning Kenyan regulatory system.

In August 2024, the Court of Appeal of the Philippines amended its April 2024 decision. The Court did so in response to motions for reconsideration. MASIPAG and Greenpeace requested reconsideration giving the following explanation to the Court of Appeals:

> "The petitioners [MASIPAG and Greenpeace] pray that this Court modify Item (8) of the (of the April 2024 judgment) on the ground of newly discovered evidence. They submitted an online BusinessWorld Article . . . on 29 April 2024 entitled, "*How may the Philippines be affected by the Court of Appeals 2024 Writ of Kalikasan?*" explaining that the Philippines imports genetically modified organisms (GMOS) such as yellow corn and soya meal, which are the most important feed ingredients in animal feeds. Since these animal feeds comprise 60%–70% of the total cost of pork, poultry meat and egg production, the Court's directive to ban GMO importation would have grave and adverse economic effect on the country's swine and poultry industries." [MASIPAG August 2024, p. 4]

The reader should note that the immediately preceding quotation is from a MASIPAG and Greenpeace document asking the Court of Appeals to reconsider Item 8 of the April 2024 order. As previously explained in the summary of the Filipino litigation, the Court of Appeal did decide to strike Item 8 from the final August 2024 Order. Why did MASIPAG and Greenpeace undermine their

own implacable opposition to genetically modified crops, foods, and feeds in the Philippines by asking for the deletion of Item 8? One can properly ask: did MASIPAG and Greenpeace change their legal stance due to newly discovered evidence, as the quotation says? Information about the massive quantity of imported genetically modified corn and genetically modified soybean, as the feed supply for the livestock industry of the Philippines, was widely and easily known prior to the April 2024 Order. Or, one can properly ask: did MASIPAG and Greenpeace reconsider because of cynical political calculations about the likely societal uproar from Filipinos who, if Item 8 were imposed, would be deprived of meat supplies and be forced to pay more for the lessened supply? The record of the litigation provides no answer to these two "one-can-properly-ask" questions. What the record does show is that by their request for reconsideration to delete Item 8 from the final August 2024 Order, MASIPAG and Greenpeace were more concerned about feeding livestock than feeding Filipinos. By contrast, MASIPAG and Greenpeace sought and won a court order that deprived Filipinos especially subsistence farmers and the urban poor–those who would most benefit from Golden Rice and Bt eggplant, – of nutritious food (Wu et al., 2021). The cynicism of MASIPAG and Greenpeace, at least to this author, seems obvious: feeding livestock is preferred to feeding Filipino people.

The Court of Appeals did modify its April 2024 Order by deleting Item 8 from its August 2024 Order. The Court reasoned that the Item (8) ban on importation of food and feed raised significant due process concerns because the importers of these foodstuffs and feedstuffs were not parties to the litigation [MASIPAG August 2024, pp. 30–31].

However, when the Court of Appeals ruled for MASIPAG and Greenpeace to delete Item 8 in August 2024, the Court did so without discussing or even citing any constitutional provisions or statutes of the Philippines or any international standards that proclaim human welfare as a worthwhile and co-equal value [Dubock, 2024, *passim*]. The Court of Appeals did not seriously consider that the Writ of Kalikasan (the Writ of Nature) might not be an absolute, predominant right in the Philippines to the detriment of human welfare. The Court of Appeals simply gave no consideration to balancing co-equal values. By endorsing the ban on Golden Rice and Bt eggplant, the Court of Appeals endorsed the legal argument that the Filipino environment is preferred to human welfare of the Filipino people.

No wonder that by May 2025 179 Nobel Laureates have signed a letter, drafted in 2016, protesting Greenpeace and MASIPAG and their campaign against agricultural biotechnology, especially Golden Rice. Further, the Laureates called for governments and international governance organizations to reject these campaigns against agricultural biotechnology. As the Laureates state: "Opposition based on emotion and dogma contradicted by data must be stopped." (Laureates Letter, 2016).

Conclusion

History will judge whether the opponents or the proponents of agricultural biotechnology better protected human health and the environment. What future historians will write and conclude is unknown and unknowable in May 2025. What is known and predictable is that the pace of scientific discovery and the expansion of scientific knowledge, related to agricultural biotechnology, will not slow. Recent examples include a new gene-editing system from Chinese scientists (Chinese scientists, 2025), detailed plant genomes (Plant Genomes, 2025), gene-edited tilapia from Brazil (Brazilian fish, 2025), plant-based foods with animal genes from Argentina (Pork-Infused Soybeans, 2025), gene-transfer from hornworts (an algae) to food crops for CO2 efficiency (Funny Little Plant, 2025).

What can also be predicted is that groups that oppose agricultural science and innovation, that mistrust regulatory agencies regarding biotechnology, that employ the precautionary principle to ban breeding techniques and their products, and that place livestock and the environment (as an abstract entity, rather than actual environments) over the welfare of people will file lawsuits. If this survey of seven jurisdictions and litigation is any guide, these lawsuits may often find receptive judges who make choices about the facts, laws, regulations, and interpretations that deny these scientific achievements to farmers and plant scientists. This survey of litigation in seven jurisdictions presents clear evidence that judges in their choices can be significant impediments to the adoption of agricultural biotechnology. This survey also presents clear evidence that judges in their choices, alternatively, can meaningfully allow a way forward for agricultural biotechnology.

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Glossary

Black's Law Dictionary (8th edition, 2004) (Garner, B. Editor-in-Chief):

Collateral estoppel	1. The binding effect of a judgment as to matters actually litigated and determined in one action on later controversies between the parties involving a different claim from that on which the original judgment was based. 2. A doctrine barring a party from relitigating an issue determined against that party in an earlier action, even if the second action differs significantly from the first one.
Injunction	A court order commanding or preventing an action. To get an injunction, the complainant must show that there is no plain, adequate, and complete remedy in law and that an irreparable injury will result unless the relief is granted.
Res judicata	1. An issue that has been definitively settled by judicial decision. 2. An affirmative defense barring the same parties from litigating a second lawsuit on the same claim, or any other claim arising from the same transaction or series of transactions and that could have been – but was not – raised in the first suit.
Vacatur	1. The act of annulling or setting aside. 2. A rule or order by which a proceeding is vacated.
Writ of Kalikasan	Writ of Kalikasan means a legal remedy available to any natural or juridical person, entity authorized by law, people's organization, non-governmental organization, or any public interest group accredited by or registered with any government agency, on behalf of persons whose constitutional right to a balanced and healthful ecology is violated, or threatened with violation by an unlawful act or omission of a public official or employee, or private individual or entity, involving environmental damage of such magnitude as to prejudice the life, health or property of inhabitants in two or more cities or provinces. (Rules of Procedure for Environmental Cases A.M. No. 09-6-8-SC Rule 7, Sec. 1) "Kalikasan" is a Filipino word which in English, means "Nature". http://notocoal.weebly.com/writ-of-kalikasan.html.

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EDITED BY
Segaran P. Pillai,
United States Department of Health and Human Services, United States

REVIEWED BY
Eric M. Hallerman,
Virginia Tech, United States
Shuichi Nakai,
Bayer Crop Sicence, Japan

*CORRESPONDENCE
Monica Garcia-Alonso,
mgarcia@estelconsult.com
Petra Kostolaniova,
petra.kostolaniova@croplifeeurope.eu

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Challenges and opportunities in the regulatory landscape of genetically modified crops in the European Union

Monica Garcia-Alonso[1]*, Esteban Alcalde[2], Ine Criel[3], Concepción Novillo[4], Petra Kostolaniova[5]* and Nancy Podevin[6]

[1]Estel Consult, Bracknell, United Kingdom, [2]Syngenta, Brussels, Belgium, [3]BASF, Ghent, Belgium, [4]Bayer, Madrid, Spain, [5]CropLife Europe, Brussels, Belgium, [6]Corteva Agriscience, Brussels, Belgium

Genetically modified (GM) crops, introduced in the mid-1990s, have undergone extensive scientific scrutiny over the past three decades. While initial regulatory frameworks were stringent due to the nascent nature of the technology and uncertainty regarding their safety, subsequent comprehensive research and independent risk assessments have consistently affirmed their safety for human, animal, and environmental health, leading to widespread global adoption. GM crops have demonstrably enhanced agricultural productivity, mitigated environmental impacts associated with conventional farming, and contribute to the United Nations Sustainable Development Goals. Consequently, many nations have refined their regulatory approaches based on accumulated scientific evidence. However, the European Union (EU) presents a contrasting scenario. Despite significant investments in agricultural biotechnology research and a commitment to the Sustainable Development Goals, the EU's regulatory landscape for GM crops has become increasingly complex, effectively limiting European farmers' access to these technologies. The EU heavily relies on imports of GM-containing protein-rich crops, while its farmers cannot benefit from their cultivation. The current pre-market assessment for GM crop import and food and feed use authorization is characterized by its lengthy, costly, and unpredictable nature. This paper discusses some of the issues faced by developers when trying to obtain import approvals for GM crops in the EU and the impact that the current regulatory framework is having on innovation. The authors propose a series of practical and feasible adjustments that could be implemented during the EU's risk assessment process to unlock the benefits of biotechnology for European agriculture without compromising safety standards.

KEYWORDS

Genetically modified crops, regulatory framework, risk assessment, precautionary principle, proportionality, right to good administration

Introduction

Agricultural biotechnology was a nascent technology in the early 1990s, with the first genetically modified (GM) crops entering the food market in 1996. At the time, there was uncertainty regarding their potential safety impacts on humans, animals and the environment, and this led to many countries setting stringent regulatory frameworks, many of which were initially based on the precautionary principle. Now nearly

three decades later, GM crops have been planted in 27 countries over 209.8 million hectares (Agroinvestor, 2025). Extensive research has shown that GM crops have increased global production of food, feed and fibre and have assisted farmers in reducing the environmental impact associated with their crop protection practices and carbon emissions (Brookes, 2022; Brookes and Barfoot, 2020). Hundreds of independent risk assessments conducted by regulatory authorities worldwide have consistently concluded that GM crops are as safe as their conventional counterparts for human and animal consumption and for the environment (Goodman, 2024; Smyth et al., 2021). Consequently, many countries have streamlined their regulatory framework for GM crops, considering scientific evidence and their own regulatory experience. Unfortunately, this has not been the case in the European Union (EU), where GM crop regulations kept increasing in complexity over time (Garcia-Alonso et al., 2022).

The benefits delivered from the adoption of GM crops align with the United Nations Sustainable Development Goals (SDGs) (Lee et al., 2016). The EU has fully committed to achieving these SDGs and has invested in scientific, technological, and industrial excellence with the aim of fostering innovation to fulfil these goals (European Commission, 2024a; European Commission Directorate-General for Research and Innovation, 2010). However, despite substantial investment in research and development, most European farmers do not have access to GM crops. This is primarily due to the regulatory oversight for these products posing major challenges for developers (Masip et al., 2013; Raybould and Poppy, 2012). In contrast, the EU depends heavily on the importation of protein-rich crops from the Americas. Given the high adoption rate of GM crops outside the EU, most of these imported commodities inevitably contain GM crops. Consequently, while food and feed derived from GM crops is consumed in the EU, EU farmers cannot benefit from this technology and remain reliant on traditional crop protection methods or agricultural practices with higher environmental impacts (Masip et al., 2013).

Under EU legislation, food and feed products containing or produced from GM crops undergo a pre-market assessment for import authorisation. This process is lengthy, costly and unpredictable (Garcia-Alonso et al., 2022), an issue that the European Commission (EC) has identified as a key challenge to be addressed for fully utilizing biotechnology innovation to enhance EU industrial competitiveness and sustainability (European Commission, 2022; European Commission, 2024a).

While a legal review of the current GMO regulations for GM plants in the EU is not anticipated in the short-term, practical adjustments to the current system, particularly to the risk assessment process, are feasible without compromising safety.

This paper offers an industry perspective of the regulatory hurdles faced by developers of GM crops in the EU, explores the global implications of these challenges, and discusses opportunities for adaptations within the existing legal framework.

EU regulatory landscape for GM crops

The introduction of GM crops in the late 1990s coincided with unrelated food crises in Europe, such as bovine spongiform encephalopathy (BSE), contributing to a decline in public trust over scientific advice and governance that resulted in a negative perception of EU food safety oversight. This was particularly punitive for GM crops, a nascent technology at the time, where stringent regulations based on the precautionary principle were introduced (Anyshchenko and Yarnold, 2021; Garcia-Alonso et al., 2022). Over time, EU GM crop regulations increased in complexity culminating with the introduction of the Commission Implementing Regulation (EU) No 503/2013 (European Commission, 2013), hereafter referred to as the Implementing Regulation. This regulation, based on the European Food Safety Authority (EFSA) guidance developed in 2011 (EFSA, 2011b), made data requirements for GM crop risk assessment legally binding and introduced additional requirements, such as mandatory animal testing (Garcia-Alonso et al., 2022).

The European Union's primary legislation establishes fundamental principles that apply to all sectors regulated under its jurisdiction. These principles encompass the precautionary principle (European Commission, 2012b), the principle of proportionality (European Commission, 2012b), and the right to good administration (European Commission, 2012a). EU legislation also underscores core values such as animal welfare, the reduction of animal testing, and the efficiency and sustainability of risk assessments, and is currently encouraging activities that support regulatory simplification aimed at boosting innovation (European Commission, 2010; European Commission, 2022; European Commission, 2024a; European Commission, 2024b).

The precautionary principle, as defined in Article 191 of the Treaty on the Functioning of the European Union (European Commission, 2012b) allows for preventative action in the face of potential risk uncertainty to prevent harm to the public or the environment. It is relevant when scientific evidence is inconclusive and there are concerns about potential adverse effects, but not when sufficient scientific evidence exists, and the risk assessment body has not identified unacceptable levels of uncertainty.

The principle of proportionality, as laid down in Article 5(4) of the Treaty on European Union (European Commission, 2012b) and embedded in the General Food Law (European Commission, 2002), mandates that regulatory burdens should be proportional to the risk that they aim to mitigate (Van der Meulen, 2010). Article 5 of the General Food Law (European Commission, 2002) also specifies that regulatory burdens must be justified by the level of risk.

The right to good administration, found in the EU Charter of Fundamental Rights (European Commission, 2012a), highlights the need for effective and sustainable risk assessments, and the Transparency Regulation (EU) 2019/1381 (European Commission, 2019) further emphasizes the importance of sustainability and efficiency in risk assessment.

The EU Directive 2010/63/EU, also known as the 3R legislation (European Commission, 2010) grounded in Article 13 on the treaties on the functioning of the EU, focuses on the reduction of the number of animals used for experimental purposes and their welfare. It promotes the Replacement, Reduction, and Refinement of animal use, ensuring that animal testing occurs only when absolutely necessary and is justifiable from a scientific or educational point.

It is the view of the authors that these principles are not applied coherently in the regulation of GM crops, especially considering the large body of scientific research supporting the inference that GM

crops are as safe as their conventional counterparts (European Commission, 2010; Devos et al., 2016; Goodman, 2024; Smyth et al., 2021). While invoking the precautionary principle may have been understandable in the early years of GM crops, it is no longer sensible to apply it after three decades of safe use. Nevertheless, the EU has not updated its approach and has instead continued adding more stringent prescription (Garcia-Alonso et al., 2022). The European Commission has recently acknowledged the need for balanced regulation (European Commission, 2024b) to promote the competitiveness of biotechnology and biomanufacturing industries, and to streamline EU legislation to reduce fragmentation, simplify regulatory processes, and accelerate time to market for biotechnology innovations (European Commission, 2024a; European Commission, 2010). This indicates a willingness within the EU to support EU scientific developments and to establish a balanced and proportionate regulatory framework for biotechnology products. Legislative changes in the EU system can be lengthy and require arduous negotiations. However, adaptations within the current legal framework to improve the regulatory process for GM crops are possible and would align with current EU goals (European Commission, 2024a). The following sections describe some of the regulatory hurdles faced by developers trying to obtain GM crop import approvals in the EU and provide examples of potential adaptations that could make the system more efficient.

Regulatory hurdles under the current EU system

In the EU, developers face significant challenges in obtaining approvals for the import and food and feed use of GM crops under the Implementing Regulation (European Commission, 2013). While this regulation generally aligns with the Codex Alimentarius guidance (Codex Alimentarius, 2009-which is followed by many other countries and international organizations) it includes additional data requirements and methodology prescriptions unique to the EU.

Applications for the authorisation of GM crop imports must be submitted to the European Food Safety Authority (EFSA) and must adhere to EFSA's administrative guidance (EFSA, 2021). EFSA performs a completeness check, ensuring that data requirements specified in the Implementing Regulation (European Commission, 2013) are met and that data have been generated according to the latest EFSA guidance documents (EFSA, 2025), which provide detailed instructions for study design, data generation and statistical analyses. If data are missing or deviate from EFSA's methods, applications are put on hold until all requirements are fulfilled. For some developers, this process takes several years.

The EC and EU Member States rely on EFSA to review these applications and conduct the risk assessments. However, EFSA's current approach limits flexibility for case-by-case assessments or risk assessments proportionate to the risk posed by a particular GM crop. This is mainly due to EFSA's interpretation of the Implementing Regulation (European Commission, 2013) data requirements and of the role that EFSA has been given by the EC in ensuring its compliance. Notably, the Implementing Regulation (European Commission, 2013) includes an article, Article 5(2), that allows developers to request exemptions (derogations) from data submission requirements if there is a valid justification. Justifications should be based on: 1) the nature of the genetic modification or product, and 2) the scientific necessity of the information for risk assessment or technical impossibility of obtaining the data required. This is referred to as the "derogation clause", which offers a viable mechanism for case-by-case adaptation of the risk assessments based on the product characteristics.

However, in practice, EFSA rarely accepts derogations. Since the Implementing Regulation came into force, EFSA has been adding more prescriptive guidance and technical papers aimed at harmonising all GM applications. The review of GM crop applications at EFSA is conducted by an independent panel of experts (GMO panel) and overseen by EFSA staff. The GMO panel is renewed every 4 years, with a time limit on participation. Over time, developers have observed that when new members join EFSA's GMO Panel, changes in interpretation and implementation may occur. These adjustments are typically connected to prospective research interests and can lead to the development of new guidance or requests for supplementary information beyond the requirements set forth by CODEX and Implementing Regulation. For developers, it is a fundamental issue as the generation of regulatory data takes years and any changes in guidance introduced while the data package is being built may result in delays, making the system unpredictable due to constantly changing goalposts.

The continuous proliferation of EFSA guidance adding more data requirements and more prescription is also driven by the aim to harmonize all applications, irrespective of their risk profile, specificity, availability of scientific data, and results of previous risk assessments. As a result, the review of applications has become a one-size-fits-all checkbox exercise. This approach is inconsistent with the case-by-case approach, EU primary legislation principles described in this paper and the EC's aspiration to streamline regulation.

Notably, this regulatory system has led to market concentration, limiting the number of developers able to navigate it successfully. Those who succeed, tend to focus on products with the potential to recoup the high regulatory costs associated with EU applications. This poses a significant challenge to market for innovative niche products or products developed by Small and Medium-Sized Enterprises (SMEs) and public institutions.

Specific examples of regulatory obstacles

Stacked GM events obtained by conventional crossing

One area that really singles out the EU regulatory approach to GM crops is the regulation of products resulting from conventional crossing of two or more GM events, commonly referred to as "stacked events" or "stacks". Most jurisdictions worldwide consider conventional breeding as a safe practice, and once the safety of a single transformation event (single GM event) is established by regulatory agencies, subsequent conventional crosses, whether with GM or non-GM varieties are generally

considered safe and do not require further regulatory oversight. In some countries additional assessment may be required if the crosses involve two or more single GM events with a reasoned scientific hypothesis for trait interactions that could potentially cause adverse effects (Goodwin et al., 2021). However, in the EU, the conventional crossing of two or more single GM events is regulated as a new GM crop.

The Implementing Regulation mandates that the risk assessment for GM stacks includes a risk assessment of each single GM event. It also requires an evaluation of the stability of the transformation events in the stacks, a comparison of the expression levels of the newly expressed proteins in the stack and each single event and an assessment of potential synergistic or antagonistic effects resulting from the combination of the single events. The Implementing Regulation also states that compositional analyses and agronomic and phenotypic comparisons with the stack may have to be conducted.

In the EU EFSA does not start the risk assessment of stack applications until the risk assessment of each of the single events has been completed (Garcia-Alonso et al., 2022). This approach has a significant impact on the review timelines. While cultivation approval for a single GM event takes on average one or 2 years in most countries, import and food and feed applications in the EU average 4 years from submission to approval (Garcia-Alonso et al., 2022). The review of stack applications in the EU takes a similar amount of time as single GM events. In addition, severe delays can occur if EFSA issues new or updated guidelines between the review of a single event and its inclusion in a stack application, as these changes are often applied retroactively and studies may have to be repeated (Roper et al., 2022).

The accumulated global regulatory experience with GM stack assessments and multiple independent studies and publications indicate that stacking GM events by conventional breeding does not increase the risk of the single events (Goodwin et al., 2021). This approach has been a long-standing policy at the United States Department of Agriculture (USDA), the United States Food and Drug Administration (FDA), Health Canada, China and the Food Standards Australia and New Zealand (FSANZ), where no additional safety assessment is conducted for stacks of previously approved single GM events. In view of the regulatory experience gained with safety assessments for stacks, some countries like Japan have updated and streamlined their regulations implementing an approach whereby familiarity with the events and types of combinations determine whether further regulatory oversight is needed (Iizuka, 2020; Kasai and Ohsawa, 2021).

Argentina has also undertaken a comprehensive review of its agricultural biotechnology regulatory policies, drawing on its extensive experience and continuous engagement with advances in scientific knowledge. This revised framework has led to more streamlined and predictable oversight procedures, greater accessibility for small and medium-sized enterprises and academic institutions seeking approvals, and an expanded diversity of approved events and crop species (Lewi et al., 2025).

Streamlining the risk assessment for stacked events obtained by conventional crossing would align with the current EU principles and objectives mentioned above (European Commission, 2010; European Commission, 2022; European Commission, 2024a; European Commission, 2024b). These products are grown in cultivating countries, as they are considered valuable tools for sustainable agricultural production. Delays in obtaining approvals in the EU lead to trade issues and hinder innovation.

Given EFSA's extensive experience with stacked events reviews and the well-documented safety of conventional crossings, streamlined procedures should be considered for stacked events obtained by conventional crossings for which the risk of the parental events was assessed by EFSA, without compromising safety. Following the Implementing Regulation, stack submissions could comprise cross-references to relevant data previously submitted for each single event, data on stability and expression, and an assessment of potential interactions between events that could impact food and feed safety. These initial assessments would determine whether additional data on the stack (e.g., composition or agro-phenotypic comparisons) are warranted. Derogations for any study that would not be necessary from a scientific point of view should be accepted. This approach would be more in line with the EU principles of proportionality and good administration and the EC's aim to simplify regulatory procedures that foster innovation in biotechnology. It would also align with the approach used in other countries, such as Japan, Brazil, and Argentina, where data on stacks is not required unless interactions that could lead to adverse effects have been identified. It is imperative to note that to this date, interactions between traits present in different GM single events in a stack have not been identified or reported.

Balancing animal welfare and scientific risk assessment needs

The Implementing Regulation mandates animal testing for all new single GM events (European Commission, 2013). This EC requirement was aimed at facilitating consensus among Member States (Garcia-Alonso et al., 2022), and therefore was driven by political motives rather than scientific reason. This requirement has been a subject of ongoing debate. EC-funded research programmes concluded that 90-day feeding studies for GM crops do not add valuable data to risk assessments in the absence of a clear testing hypothesis (European Commission, 2018). EFSA has supported these conclusions on multiple occasions (Devos et al., 2016), but also interpreted the EC decision as a *de-facto* regulatory requirement for all GM single events (EFSA, 2011b). In addition, while international guidelines for performing 90-day rat toxicity studies have been in place since 1981 under the Organisation for Economic Co-operation and Development (OECD) umbrella (OECD, 1998), EFSA opted to publish their own guidelines in 2014 (EFSA, 2014). This rigidity has led to situations where EFSA has rejected studies performed under OECD guidelines and requested that the studies be performed using EFSA methodology.

An example is provided in Roper et al. (2022), where a 90-day rat feeding study had been performed to support the application for food and feed approval of GM maize line TC1507 in 2002. The study was compliant with OECD guidelines (OECD, 1998) and EU regulatory requirements at the time. The study was evaluated by EFSA and considered acceptable, consequently, TC1507 was approved in the EU in 2004. The same study was later used to support stack applications containing TC1507 and accepted. However, when more applications for approval of stacks

containing TC1507 were submitted in 2015, EFSA requested a new 90-day rat feeding study, arguing that the existing study did not comply with the latest EFSA guidance (EFSA, 2014) and therefore could not support a risk conclusion. A derogation based on the fact that a valid study already existed was not accepted. This represents a clear deviation from EU principles, especially from the 3R legislation (Replacement, Reduction and Refinement of animal use) (European Commission, 2010).

Considering the reaffirmed EU commitment to phase out the use of animals for testing purposes, an alignment between the EC, EU Member States, and EFSA is imperative. A practical short-term solution would be for the EC to enable EFSA to conduct science-based, case-by-case risk assessments, where studies that follow international guidelines and are scientifically sound, are accepted, even when the guidelines deviate from EFSA guidance. Also, there is abundant scientific evidence that confirms that 90-day rat feeding studies do not add value to risk assessments, unless there is a clear risk hypothesis (Devos et al., 2016; European Commission, 2018). Article 5 in the Implementing Regulation 503/2013 could be used to accept derogations.

Comparative assessment of crop composition in the EU

In the EU, deviations from primary legislation principles are also evident in the comparative assessment conducted to analyse and compare crop composition. These studies are recommended by the Codex Alimentarius guidelines (Codex Alimentarius, 2009) as part of the hazard identification process for food safety assessments. The aim is to compare the composition of key nutritional parameters in a conventional crop with the GM version of the crop to determine whether the genetic modification has led to unintended changes in composition. Samples for analyses are collected from regulatory field trials and analysed in certified laboratories.

While most countries request these studies only for GM single events, EFSA also requests these studies for stacks. In addition, there are remarkable differences in how these studies are conducted in the EU and in the rest of the world. As previously discussed, the Implementing Regulation (European Commission, 2013) was based on existing EFSA guidance, providing detailed instructions on the design and statistical analyses to follow for compositional analyses (EFSA, 2010; 2011a), which has since been complemented with further guidance (EFSA, 2015; 2018). For instance, the studies must be conducted at a minimum of eight sites, with four replicates per site (8x4) and must include a comparison of the GM plant with its conventional counterpart and with a minimum of three non-genetically modified reference varieties of the crop per site (with a minimum of six over the whole study). When genetically modified plants possess herbicide-tolerant traits, composition data are required for both treated and untreated GM entries. This translates to a minimum of five entries, replicated four times on at least eight sites, resulting in 160 entries for which approximately 80 analytes (in the case of maize) are measured, leading to a minimum of 12,800 analyses. Should weather conditions or other circumstances compromise sample collection from any plot, EFSA deems the data set incomplete and requests additional data, leading to long delays and increased costs. Consequently, applicants routinely add extra sites, replicates, and/or number of commercial references. However, even when the number of entries for each line exceeds that derived from a perfect 8 by 4 design and the statistical power of the experiment is higher, EFSA does not accept data which does not meet the perfect 8 by 4 requirements.

In contrast, other countries make risk assessment conclusions based on expert judgement of studies that may include fewer sites and/or replicates, provided that the study design is scientifically sound (Brune et al., 2013) and do not impose the requirement of adding extra conventional varieties. A typical study may have two entries (GM and comparator), four replicates per entry at four sites (32 entries), resulting in 2,560 analyses, five times less than the minimum requirement in the EU. The results are then put into the context of natural variability (Codex Alimentarius, 2009) using the Crop Composition Database (AFSI, 2024), which contains compositional data on hundreds of varieties of many crops, to ascertain the biological relevance of any differences found. In contrast, EFSA imposes a complex statistical analysis that not only tests the hypothesis of no difference to the conventional counterpart, but also the equivalence of the GM crop with at least six reference varieties included in that study. This approach results in a variety of potential outcomes regarding differences and equivalences, with limited added value for the risk assessment. This begs the question of why EFSA cannot make a risk conclusion when a dataset is not produced exactly as prescribed when regulatory authorities around the world can reach a conclusion with a fraction of the data.

Furthermore, the EU is the only jurisdiction where such complex compositional analyses for stacked events are mandated. The costs and time associated with this endeavour can be borne only by large companies for products with a substantial market share. Smaller developers or developers of products that primarily focus on addressing challenges in niche markets are discouraged by this regulatory requirement, effectively hindering innovation.

Experience accumulated over 30 years supports the fact that genetic modifications introduced in commercial GM crops to date have not resulted in unexpected alterations of crop composition, while at the same time, differences can be clearly found between different conventional varieties of the same crop (Herman and Price, 2013).

This illustrates that EU's mandatory data requirements conflict with the EU principles of proportionality and good administration and certainly do not align with regulatory simplification. It also shows that the acceptability of data by EFSA is contingent upon literal compliance with the Implementing Regulation and the prescribed EFSA methodology. There are, however, potential approaches that could be adopted by EFSA to improve the efficiency of the review process:

- For single GM events, existing compositional analyses conducted in the countries where these events were approved for cultivation could be accepted in the EU for import applications, even if the studies were not conducted in accordance with EFSA guidance. This approach would avoid duplication of data without compromising safety assessments. Aligning with the rest of the world would alleviate the burden

associated with this intricate study design and result in data packages more representative of the level of risk posed by these products.

- For GM stacks where compositional analyses conducted with the single events have not revealed any biologically relevant changes in composition, and interactions among the single GM events that could lead to adverse effects relating to food or feed are unlikely, compositional analyses with the stack should not be mandatory. Extensive scientific evidence and a large number of compositional studies with stacks reviewed by EFSA confirm that conventional crossing of single events does not result in relevant compositional changes in stacks. In this case, the derogation clause could be used to avoid generating large data sets that are unlikely to provide additional information for the risk assessment.

These adaptations would be in line with the EU principles of proportionality and good administration and the EC's aim to simplify regulatory procedures.

Discussion and proposals for improvement

Scientific evidence and regulatory experience accumulated over the last three decades have shown that GM crops are as safe as their conventional counterparts. While polities that foster innovation in agricultural biotechnology have leveraged this experience and streamlined their regulatory oversight for these crops, the EU has continued to apply an overly precautionary approach that has led to regulations that deviate from key EU principles that are supposed to be applied across all regulated sectors. While the Implementing Regulation introduced in the EU in 2013 (European Commission, 2013) was intended to improve the approval process, its legally binding nature combined with the way in which it is currently implemented by EFSA has resulted in a cumbersome, costly, unpredictable and lengthy regulatory system, disproportionate to the risk posed by these products. More specifically, the current regulatory system does not build on the accumulated scientific evidence and regulatory experience gained over the last three decades and is not aligned with current EU objectives that aim at regulatory simplification to foster innovation in biotechnology.

While a legal review of the current legislation for GM plants in the EU is not anticipated in the short-term, practical adjustments can be made to modernise and streamline the regulatory process without compromising on safety. This is particularly important considering the pressing need to address global food supply challenges and the rapid pace of scientific discoveries, which are yielding new products that can significantly contribute to alleviate those challenges, benefiting both farmers and consumers.

A key tool at hand is Article 5 on derogations in the Implementing Regulation (European Commission, 2013). Its use could streamline risk assessments within the current regulatory framework, but this would require closer alignment between EU risk assessors (in EFSA) and risk managers (in the EC). Currently, EFSA appears to operate within the constraints of the mandatory and legally binding nature of the Implementing Regulation. As discussed in this paper, this approach has resulted in a trend where conducting science-based case-by-case risk assessments, proportionate to the risk posed by a particular product, is just not possible. Instead, EFSA has opted for a "harmonization" approach to ensure compliance, where it is expected that all GM applications for import and food and feed approval contain the same data, and that the data has been generated in the same prescribed manner. By enabling EFSA's application of more modern approaches in risk assessment, building on scientific evidence and allowing the use of Article 5 on derogations, the EU could move closer to its aim of fostering innovation in this area. This would also result in assessments aligned with the EU principles used in other EU regulated products sectors and international best practices.

There are several ways in which the current regulatory system for GM crops could be improved within the existing legal framework:

- Streamlining the review for stacked products produced by conventional crossing.
  - Following a stepwise approach, where the data mandated by the Implementing Regulation for all stacks (genetic stability, expression and potential interactions) is examined and used to determine whether additional data is necessary.
  - Allowing the use of Article 5 derogations when there is scientific justification for not conducting additional studies.
- Aligning the risk assessment of GM crops with the 3R regulation that supports animal welfare and aims at minimising the use of animal testing.
  - Accepting existing animal studies conducted following international guidelines to avoid unnecessary duplication of studies.
  - Allowing the use of Article 5 on derogations when there is a scientific justification for not conducting such studies.
- Adopting a standardized approach for evaluating the reliability of study data across all regulated food areas, based on scientific principles such as the Klimisch score (Klimisch et al., 1997).
  - Aligning EFSA's approach with other EU risk assessment bodies, ensuring that scientifically sound results are appropriately considered in risk assessments, even if they deviate from EFSA's prescribed methodology.
- Ensuring a high level of competency in risk assessment methodologies in all personnel and panel experts involved in the review of GM crop applications. This would avoid questions and data requests driven by scientific curiosity rather than risk assessment best practices ("need to know" versus "nice to know" (Raybould et al., 2012)).

The authors acknowledge that EFSA is currently exploring ways to introduce regulatory simplification and are reviewing the extensive list of guidance documents with the aim to provide clearer procedures for developers. This effort is critical and should consider alignment with international best practices and approaches used by other EU risk assessment bodies. With some practical adjustments in the implementation of the current regulation for GM crops, the EU has the opportunity to move towards greater regulatory efficiency and unlock the current barriers to innovation in agricultural biotechnology, without compromising on consumer, animal and environmental safety.

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MG-A: Writing – review and editing, Conceptualization, Writing – original draft. EA: Writing – original draft, Writing – review and editing. IC: Writing – original draft, Writing – review and editing. CN: Writing – review and editing, Writing – original draft. PK: Writing – review and editing. NP: Conceptualization, Writing – original draft, Writing – review and editing.

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EDITED BY
Carmen Vicien,
University of Buenos Aires, Argentina

REVIEWED BY
María Fabiana Malacarne,
Asociación Semilleros Argentinos, Argentina
Clara Rubinstein,
Institute for Scientific Cooperation in Environment and Health (ICCAS), Argentina

*CORRESPONDENCE
Leah Buchman,
lebu@novonesis.com
Emma Kovak,
ekovak@thebreakthrough.org

†These authors have contributed equally to this work and share first authorship

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A call for congressional action: revisiting the U.S. coordinated framework for the regulation of biotechnology

Leah Buchman[1,2*†] and Emma Kovak[3*†]

[1]Novonesis A/S, Washington, DC, United States, [2]Georgetown University, Washington, DC, United States, [3]The Breakthrough Institute, Berkeley, CA, United States

Since the 1986 release of the Coordinated Framework for the Regulation of Biotechnology almost 40 years ago, there have been two whole of government updates that made only minor changes, while new regulations and guidance from individual agencies have made more substantial alterations. Despite scientific advances and the emergence of products that fall outside the purview of legacy statutes, repeated calls for substantive changes have gone largely unanswered. We expand upon the NSCEB's most important recommendations for improvements to the Coordinated Framework. We recommend that Congress create an NBCO and direct it to create a centralized application submission portal; conduct horizon scanning for future products of biotechnology; streamline regulations for familiar products and exempt low-risk products; and improve organizational structure, staff training, and interagency exchange.

KEYWORDS

biotechnology, CRISPR, innovation, coordinated framework, agriculture, national security, GMO, gene editing

Introduction

Lead up to the Coordinated Framework

The emergence of recombinant DNA (rDNA) technology in the early 1970s marked the beginning of a new era in molecular biology, enabling scientists to isolate, cut, and recombine genetic material across species boundaries. As researchers began to explore the applications of these new techniques, ethical, environmental, and safety concerns were raised about their potential implications. During the 1973 Gordon Research Conference on Nucleic Acids, leading scientists expressed apprehension over the unknown consequences of rDNA experimentation. In the aftermath, a group of prominent researchers sent a letter to the National Academy of Sciences, Engineering and Medicine (NASEM), calling for a temporary moratorium on certain types of rDNA research and urging the development of safety protocols (Berg et al., 1974).

The call for safety protocols led to the 1975 Asilomar Conference on rDNA, a seminal event where over 100 scientists, lawyers, and journalists gathered to develop consensus guidelines for the safe conduct of rDNA research (Berg et al., 1975). The resulting "Asilomar Guidelines" emphasized containment, risk assessment, and self-regulation, establishing a precedent for proactive governance of emerging biotechnologies. These guidelines were quickly institutionalized when the National Institutes of Health (NIH) issued the first

version of the *NIH Guidelines for Research Involving Recombinant DNA Molecules* in 1976, formalizing oversight for federally funded genetic engineering research (NIH, 1976).

While early regulation focused largely on containment within laboratory settings, rapid advances in biotechnology throughout the late 1970s and early 1980s, along with the increasing involvement of private industry, raised new questions about environmental release and commercialization. The 1980 Supreme Court decision in *Diamond v. Chakrabarty* allowed genetically engineered organisms to be patented, a watershed moment in biotech regulation (Diamond v. Chakrabarty, 1980). It spurred a wave of commercial investment and accelerated the push toward field testing and market deployment of genetically modified organisms (GMOs), including agricultural crops and microbial products.

By the early 1980s, developers were requesting approval to conduct field trials of genetically modified organisms, but no unified federal framework existed to assess their potential environmental or public health impacts. A series of reports and initiatives attempted to fill this gap (NRC, 1984; NRC, 1987). At the same time, legislative attention intensified. Senators Albert Gore Jr. and Bill Owens proposed a more structured public oversight regime, emphasizing transparency, public trust, and inter-agency coordination (Gore and Owens, 1984).

The Coordinated Framework

The developments above culminated in the 1986 release of the *Coordinated Framework for the Regulation of Biotechnology* (hereinafter referred to as the 'CF'), published by the White House Office of Science and Technology Policy (OSTP, 1986). The CF was not a new regulatory statute but rather a policy interpretation of how existing federal laws, such as the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Federal Food, Drug, and Cosmetic Act (FDCA), the Toxic Substances Control Act (TSCA) and the Plant Protection Act (PPA) would apply to biotechnology products. The CF primarily allocated responsibility among the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA). The CF emphasized a product-based approach, asserting that oversight should be based on the characteristics and risks of the final product, not the method used to produce it. The CF was designed to promote innovation by leveraging existing statutory authorities rather than creating new biotechnology-specific legislation.

In 1992, OSTP issued an update of the CF that reiterated the product-based focus and affirmed that existing laws were sufficient to ensure safety. The update also refined the criteria for risk assessment and stressed that regulatory review should be commensurate with risk, while reaffirming the need for inter-agency coordination (OSTP, 1992). A second major update was released in 2017 and called for improved clarity, transparency, and public engagement but did not fundamentally alter the legal or institutional architecture of the framework (OSTP, 2016; OSTP, 2017).

Researchers have debated that while the 1992 and 2017 updates introduced new language, refinements in scope, and procedural guidelines, they did not meaningfully revise the underlying regulatory logic or redistribute agency responsibilities (Kuzma et al., 2008; Ahmad et al., 2024). The USDA, EPA and FDA have reasonably effectively adapted their statues to cover a wide range of

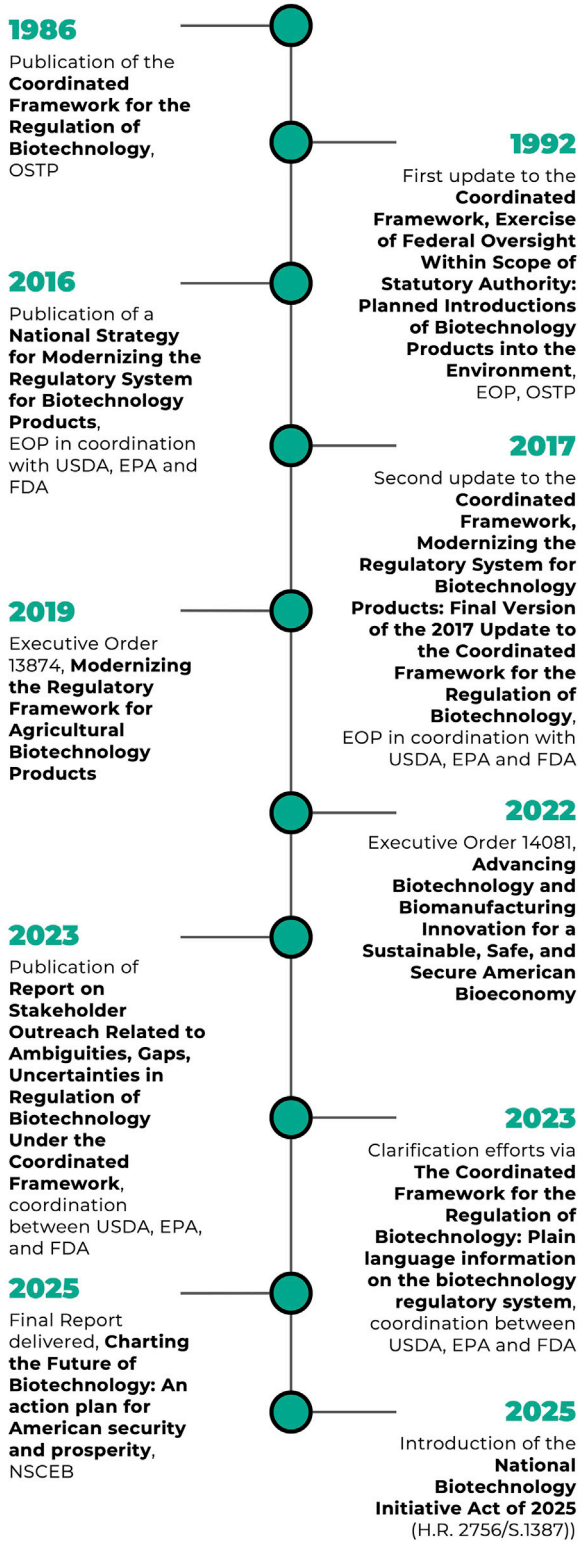

FIGURE 1
Timeline of changes to the Coordinated Framework (CF) and enabling actions.

products. However, the core reliance on pre-existing statutes has limited the framework's adaptability to novel biotechnologies that fall outside the clear purview of legacy laws, such as engineered gene drives. Despite repeated calls for greater interagency coordination and updated regulatory processes, no significant legislative overhaul has occurred, and the 2017 CF remains the foundational policy instrument for biotechnology regulation in the U.S. (Figure 1).

Executive-led biotechnology recommendations and actions

Recently in the U.S., biotechnology regulation has been shaped significantly by presidential administrations, reflecting evolving priorities around innovation, safety and global competitiveness. In 2019, President Donald Trump signed Executive Order (EO) 13874, which emphasized reducing regulatory burdens and promoting American leadership in agricultural biotechnology (USDA, 2019). The order directed agencies to adopt risk-proportionate, science-based regulation and to eliminate duplicative or overly burdensome steps in the approval process. This EO supported USDA's efforts to implement the *SECURE* rule, finalized in 2020, which revised the agency's oversight of genetically engineered organisms; the *SECURE* rule was vacated in December 2024 following a district court's decision on a lawsuit challenging the rule (National Family Farm Coalition v. Vilsack, 2024).

President Joe Biden's 2022 EO 14081 marked an expansion in the scope of biotechnology administration interest (Federal Register, 2022). Reflecting both economic and security concerns, it positioned biotechnology not only as a field of scientific inquiry but as a strategic sector critical to supply chain resilience, national defense, and climate mitigation, calling for a comprehensive bioeconomy strategy, updated regulatory paradigms for emerging biotechnologies (e.g., synthetic biology, engineered microbes), and cross-agency coordination to foster safe, ethical innovation.

The National Security Commission on Emerging Biotechnology (NSCEB) and the case for institutional modernization

Congress created the National Security Commission on Emerging Biotechnology (NSCEB), a bi-partisan and bi-cameral commission charged with reviewing advancements in biotechnology and assessing how they shape activities by the Department of Defense. The NSCEB frames biotechnology as a national asset integral to economic security, defense preparedness, and global competitiveness. Aimed at identifying concrete steps, NSCEB developed recommendations through stakeholder engagement, and in its final report, released in April 2025, called for a more centralized and proactive governance model to ensure that the U.S. maintains leadership in a rapidly evolving technological landscape (NSCEB, 2025).

Historically, biotechnology and agricultural innovation have garnered bipartisan support in the U.S., reflecting a shared recognition of their vital roles in scientific readiness and global competitiveness (Dunn and Panetta, 2017; NSCEB, 2025). Advances in genetic engineering have been prioritized for their capacity to enhance crop resilience, boost productivity, and contribute to sustainable agriculture amid escalating climate challenges (NASEM, 2016). Moreover, the increasing recognition of agriculture and food systems as strategic national security concerns, fueled by geopolitical instability and supply chain vulnerabilities, underscores the imperative for coherent, science-based governance that balances innovation with environmental stewardship (The White House, 2022; NSCEB, 2025; USDA, 2025). Robust and proportional regulatory oversight can help the U.S. sustain its leadership in agricultural biotechnology while addressing both economic and security priorities (NSCEB, 2025).

Policy options and implications

The NSCEB report recommends approaches to improving biotechnology governance at the federal level, and Congress should follow these recommendations. This section expands upon the most important recommendations from the NSCEB.

Establish a National Biotechnology Coordination Office (NBCO)

Since the 1986 release of the CF, subsequent updates have yet to substantially alter coordination mechanisms at a high level, though agencies have made progress in coordinating regulation of specific types of products. Considering repeated calls for more coordination between agencies, the time is ripe to learn from past experiences and chart a new path forward.

One early coordination mechanism, the Biotechnology Science Coordinating Committee (BSCC), was established in an OSTP policy (50 Fed. Reg. 47,174 (1985)) ahead of the 1986 CF and ceased to function by 1989 (Shapiro, 1990). It was composed of senior staff from the five main agencies involved in biotechnology regulation and funding of biotechnology research: USDA, EPA, FDA, NIH, and NSF. The purposes of the BSCC as laid out in the 1985 OSTP policy were (50 Fed. Reg. 47,174 (1985):

1. Serve as a coordinating forum for addressing scientific problems, sharing information, and developing consensus
2. Promote consistency in the development of federal agencies' review procedures and assessments
3. Facilitate continuing cooperation among federal agencies on emerging scientific issues
4. Identify gaps in scientific knowledge

During its tenure, the BSCC struggled with conflict, some of which centered around the issue of whether some organisms should be exempt from regulation. When EPA proposed its new TSCA regulations, other agencies in the BSCC disagreed with EPA's approach and asked the Office of Management and Budget (OMB) to block the new regulations (Jaffe, 1987; Shapiro, 1990). Since the BSCC did not have statutory authority to perform its coordinating functions, it was not able to resolve this conflict between the agencies (Shapiro, 1990). To preclude similar issues from surfacing with an NBCO, one important component is clear

statutory authority for the NBCO's existence and for it to perform the specific functions outlined in the sections below. The involvement of the NBCO represents an opportunity to have fit-for-purpose regulations and guidance documents when statutory changes may not be necessary. The agencies' roles and responsibilities and involvement with the NBCO should also be codified to support implementation by agency leaders, including the role of General Councils from each agency to help decide which agency will regulate a novel product (Carter, 2023).

In April 2025, in parallel with the report publication, Congress introduced the National Biotechnology Initiative Act, H.R. 2756 (2025); S.1387 (2025), which seeks to codify several key recommendations from the NSCEB report. The bill would establish an NBCO within the Executive Office of the President (EOP), led by a presidentially appointed director tasked with coordinating biotechnology policy across federal agencies. The legislation also directs the development of a National Biotechnology Strategy, to be updated every 4 years, with a focus on economic competitiveness, regulatory efficiency, national security, and workforce development. By embedding these priorities in statute, the Act would provide durable, institutional support for a cohesive, whole-of-government biotechnology policy, reinforcing the strategic vision articulated in NSCEB's final report, and addressing past issues with the BSCC.

The call for a centralized authority in Recommendation 1.1a of the NSCEB report—a proposed National Biotechnology Coordination Office (NBCO)—would provide enduring executive leadership and strategic alignment across defense, commerce, health, and agriculture, addressing long-standing criticisms of fragmented oversight and regulatory inconsistency. After decades of calls for improved coordination, the NSCEB report's proposal for the NBCO stands out as substantive and actionable.

In the following sections we describe actions the NBCO should take to facilitate streamlining of regulations.

Centralized regulatory application submission portal

One recommendation that is not discussed in the NSCEB report is a centralized regulatory application submission portal to streamline review of biotechnology products and lessen the burden on developers. The NBCO should run such a portal, which should allow developers to submit information on a product, receive in return a list of information required for their submission package that includes requirements from all relevant agencies, and to upload the completed submission to a centralized portal. As much as possible, agencies should develop shared data standards that allow developers to submit data in one format that can be used by multiple agencies rather than submitting multiple versions of similar data required by different agencies.

A single point of entry into the regulatory system would simplify risk assessment and management by directing products to the appropriate agencies and increasing transparency for developers and the public (NASEM, 2017; Chemla et al., 2025). Beyond serving as a submission platform, the portal would act as a collaborative workspace where agency reviewers can communicate directly with each other about a product. Shared dashboards and document repositories would facilitate interagency dialogue, allowing reviewers to exchange questions, clarify data needs, and coordinate risk assessments without always needing to route communications through the developer.

Additionally, status tracking, automated notifications, and centralized documentation would improve accountability and provide developers with clear guidance throughout the regulatory process.

This coordinated approach is particularly important given overlapping jurisdictional responsibilities for biotechnology products. For instance, genetically engineered microbes used in agriculture may fall under multiple agencies: USDA-APHIS regulates under the Plant Protection Act (PPA) if the organism contains plant pest elements or could impact plant health; EPA's Office of Pesticide Programs (OPP-BPPD) oversees microbial biopesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA); EPA's Office of Pollution Prevention and Toxics (OPPT) regulates "new" microbial strains under the Toxic Substances Control Act (TSCA) if environmental exposure is possible; and FDA regulates food or feed applications associated with fermentation co-products under the Federal Food, Drug, and Cosmetic Act (FFDCA).

Streamline regulation: exempt low-risk products from unnecessary regulation

There is a critical need to modernize the regulatory landscape for products of biotechnology. Policymakers and industry stakeholders are reaching a growing consensus that the current regulatory environment often stifles innovation without yielding added meaningful safety benefits (Karsten and West, 2017; BIO, 2023). Regulations should be streamlined to apply oversight "only where the risk posed by the introduction is unreasonable," or the reduction in risk is greater than the cost (OSTP, 1992). The NBCO could ensure that USDA, EPA, and FDA regulations follow this principle.

Streamlining regulatory processes for well-understood products could also help lower barriers to entry for startups and academic ventures while maintaining rigorous oversight where unreasonable or genuinely novel risks are present. For example, FDA has conducted New Plant Variety (NPV) consultations for 81 insect resistant crops and 99 herbicide tolerant crops from 1995 to 2024 without substantially streamlining review for products similar to those the agency has previously reviewed. As a NASEM consensus report on genetically engineered crops concludes, premarket regulations should apply to "plants that express traits that are new to established, cultivated crop species and that pose a potential for environmental harm, regardless of the process used" (NASEM, 2016). Agencies should ensure their regulations exempt low-risk products, streamline regulations for organisms without new traits, and build in processes that enable agency flexibility as science and the agency's understanding and experience evolve.

Horizon scanning for future products of biotechnology

To remain competitive on a global scale and foster innovation, it is essential that regulatory structures anticipate emerging

technologies and adapt proactively rather than reactively. The NBCO should be able to horizon scan, identify new technologies, assess how they fit into the existing CF, and highlight any concerns to Congress (Dooley, 2018). Historically, regulatory agencies have responded more reactively to new technologies. For example, CRISPR-Cas9 was first used as a gene editing tool in 2012, but USDA did not finalize the SECURE rule to incorporate gene edited plants until 2020, EPA finalized regulations for gene edited plant incorporated protectants (PIPs) in 2023, and FDA issued guidance for gene edited New Plant Varieties (NPVs) in 2024.

Regulators must prepare for the next generation of novel products, many of which may not fit neatly into existing regulatory paradigms. Recommendation 2.1b of the NSCEB report suggests that Congress instruct federal agencies to proactively develop review pathways, anticipating both the complexity of products and their societal implications. Developing anticipatory governance mechanisms, including precompetitive testing frameworks for new products, adaptive risk assessment tools, and providing agencies flexibility to assess and exclude products from existing regulations as needed will be critical to avoiding regulatory lag and maintaining public trust.

The NBCO and biotechnology regulatory agencies should partner with the NASEM, which frequently conducts horizon-scanning activities to identify emerging scientific and technological trends, such as the widely cited consensus report *Preparing for Future Products of Biotechnology* (NASEM, 2017).

People, training, and interagency exchange

There are several additional recommendations in the NSCEB report that would support interagency coordination and streamlining of biotech regulation including formal leadership roles, bioliteracy, and interagency biotechnology training.

TABLE 1 Actionable recommendations.

Recommendation	Involved entities	Reasoning	NSCEB final report recommendations
Establish NBCO	Legislative Branch, Executive Branch	Creating an NBCO responsible for biotechnology regulation and oversight would enable seamless interaction between agencies. An integrated system would modernize biotechnology regulation, making it more efficient, predictable and transparent while maintaining rigorous safety and environmental standards	Recommendation 1.1a urges Congress to establish a National Biotechnology Coordination Office (NBCO) within the Executive Office of the President, led by a presidentially appointed director, to coordinate interagency efforts concerning biotechnology competition and regulation
Appoint senior biotech leadership in agencies	NBCO, USDA, EPA, and FDA	Designate senior officials in each agency responsible for biotechnology governance and interagency coordination. Dedicated biotechnology leaders embedded within agencies will help institutionalize best practices, sustain bioliteracy, and support coherent policy execution	Recommendation 1.2a proposes that Congress require each relevant federal agency to designate a senior official responsible for leading biotechnology policy
Centralized application submission portal	NBCO, Regulated Industry, USDA, EPA, and FDA	Develop and manage a unified portal for biotechnology product submissions. This would help to reduce duplicative requests, align review timelines, and enable the formulation of cross-agency working groups to address complex scientific or regulatory issues	N/A
Streamlining regulation	NBCO, USDA, EPA, and FDA	Remove redundant or unnecessary regulatory steps, particularly for well understood products. This is part of ensuring that regulations yield meaningful safety benefits, meaning the reduction in risk is greater than the cost	Recommendation 2.1a calls for Congress to direct federal regulatory agencies working through the EOP to create simple, predictable pathways to market and to exempt familiar products from unnecessary regulation. The NSCEB report claims that agencies lack statutory authority to reduce regulation for well-understood products and instead must evaluate each product on a case-by-case basis whether it is familiar or novel AND Recommendation 2.1b (below)
Horizon scanning	NBCO, NASEM	Engage independent scientific bodies to assist in identifying and assessing emerging biotechnologies. Productive reports involve diverse stakeholders including from academia, small and large companies, national laboratories, and foundations	Recommendation 2.1b highlights the importance of preparing for new products of biotechnology and recommends that Congress instruct federal agencies to proactively develop review pathways, anticipating both the complexity and societal implications of future products. These biotechnologies may include synthetic organisms with no clear comparator organisms, programmable biologics, or distributed biomanufacturing platforms
Build and maintain interagency workforce capacity	NBCO, USDA, EPA, and FDA	Develop ongoing biotech training and capacity building across the federal workforce. Formalizing leadership and ensuring ongoing training and knowledge sharing can promote interagency exchange and workstream efficiency	Recommendation 5.1a suggests that Congress mandate that OPM implement biotechnology-specific training programs across federal agencies to build interagency capacity

Effective biotechnology governance depends not only on robust processes and systems but also on the people who implement them. A key step toward improving coordination and policy coherence is addressed in Recommendation 1.2a of the NSCEB report, which suggests designation of agency biotech policy officials. These formal leadership roles would help overcome personality and organizational challenges that can impede interagency collaboration by providing clear points of accountability and communication. Even if regulations remain unchanged, the degree of effort, engagement, and coordination can vary significantly depending on the expertise and commitment of individual employees. For this reason, codifying the CF is essential to ensure consistent implementation and legally define the scope of collaboration regardless of staffing changes. Intra-agency coordination, including career staff, political appointees, and agency divisions should be prioritized as well.

Bioliteracy—the understanding of biotechnology science and policy—is critical across the federal workforce, especially as personnel inevitably change over time. The NSCEB highlights related workforce imperatives in Recommendation 5.1a, suggesting that Congress direct the Office of Personnel Management (OPM) to provide interagency biotechnology training to build and maintain critical expertise. This change would enhance regulatory capacity, support regulatory streamlining of well-characterized biotechnology products, and provide regulators with opportunities to learn about emerging technologies.

It is important to acknowledge that agencies such as USDA, EPA, and FDA have demonstrated exceptional coordination over the past several years, successfully navigating complex regulatory challenges and engaging constructively with stakeholders (USDA, EPA and FDA, 2023; USDA, EPA and FDA 2025). Sustaining this momentum requires formalizing leadership structures and ensuring knowledge sharing to promote interagency exchange. This approach will strengthen U.S. capacity to regulate biotechnology effectively and preserve the nation's competitive edge in this rapidly evolving field.

Actionable recommendations

Actionable recommendations are listed in Table 1.

Conclusion

The recommendations in this article from the authors and those from the NSCEB report reflect a shift away from the reactive governance model that characterized early biotech regulation and toward a more strategic, whole-of-government approach. They echo executive actions from the last nearly 40 years that emphasized the need for a sustainable, secure bioeconomy supported by interagency coordination, infrastructure investment, and regulatory modernization (USDA, 2019; Federal Register, 2022). Yet unlike EOs, codifying these recommendations through congressional action would provide the legal and institutional permanence necessary to navigate the challenges of the coming decades.

As with earlier turning points in U.S. biotechnology governance from the Asilomar Guidelines to the CF, the NSCEB's final report should serve as the foundation for 21st century biotechnology policy strategy. By establishing enduring structures for leadership, streamlining regulatory pathways, and preparing for the complexity of emerging products, these recommendations offer a path forward for enabling responsible innovation. Their implementation will be essential not only for sustaining U.S. competitiveness in the global bioeconomy, but for safeguarding national security in an era when biology, information, and manufacturing are increasingly intertwined.

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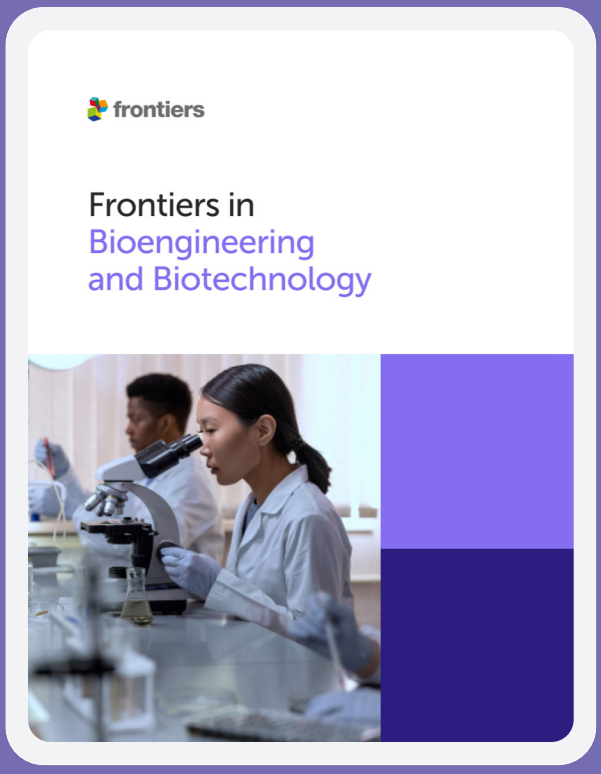

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