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Socio-Economic Considerations and their Potential Implications for Gene-Edited Crops

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Abstract

Regulatory clarity and efficiency are increasingly important for the successful commercialization of technologies resulting from public and private research and development investments. This article examines recent developments in the movement away from mostly science-based risk assessment regulatory and variety approval systems focusing on human and animal health and environmental safety to hybrid systems that include assessment of socio-economic considerations allowed for under the auspices of the Cartagena Protocol on Biosafety. We propose that socio-economic consideration assessments can be grouped into three methodological categories: empirically based, legally grounded, and consensus approaches. Our exploration of developments in the three categories reveals gaps in data, consistency, and methodology rigor that must be addressed for efficient and reliable socio-economic consideration assessment. We assess the potential impacts of these gaps on the regulation of gene-edited crop varieties, concluding that if gene-edited crops are regulated as genetically modified crops, they will endure the same fate, that is, lengthy regulatory approval processes and failure to be commercialized. The result being that the regulatory burdens in potentially adopting and food insecure countries will prevent important new crop varieties from reaching farmers and producers for their use.

Keywords: barriers to innovation, Cartagena Protocol on Biosafety, innovation, risk, gene-edited crops

1. Introduction

The regulation of agricultural innovations including plant breeding technologies such as genetic modifications continues to challenge policymakers. This challenge can be observed through the wide range of regulatory responses that have developed. In the late 1990s, the world aligned into essentially two broad groups. While both groups regulate genetically modified (GM) crops based on scientific risk assessments and variety approval processes, they differ in their emphasis of the precautionary principle. Therefore, while the first group, including Argentina, Australia, Brazil, Canada, South Africa, and the United States, have adopted many GM varieties, the second group has not. This second group includes the European Union (EU), India, and many African and Asian countries. For example, regulatory gridlock has developed within the EU as only a single crop variety has received approval for commercial use dating to 2003. Comparably, 4,485 regulatory risk assessments resulting in approval have been completed globally since 1992, involving 29 different crop types and 403 traits [35]. These science-based risk assessments have resulted in the approval of various GM crops that are presently produced in 29 countries. India, as well as African and Asian countries, have similarly rejected crop varieties that have been produced in other countries for 25 years without incident. Greater emphasis of the precautionary principle in some countries has prevented approval.

Implementation challenges and the global rift in regulation appear to be continuing as plant breeding technologies move from genetic modification to gene editing [63]. Gene editing, a recent technology, is a portfolio of different techniques that enable the possibility of improving crops and other organisms with and without changes in DNA. In those cases where there is a change in DNA, this could be done through targeted, controlled, and specific within-genome genetic changes that may include transient or temporary insertion of foreign DNA. Gene editing techniques are more precise compared to the random, uncontrolled mutations of earlier technologies such as chemical or radiation mutagenesis or, in some cases, the random insertion of foreign DNA such as with GM varieties.

Gene-edited (GEd) crops are already commercially produced in Canada and the USA, with regulatory agencies in numerous other countries indicating that if no foreign DNA is

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permanently present in the new plant variety that will be available to producers, it is eligible to be regulated as a conventional plant variety [40, 64] Crucially, this means that such plants will not be subject to the additional regulatory requirements that many countries have implemented for assessing the risks of GM crops.

Policy-maker challenges arise in countries that have indicated that GEd crops will be subject to the same regulations as GM crops. Challenges include, for example, how to regulate and differentiate those GEd crops that are physiologically indistinguishable from conventional mutagenic varieties and those with transient (foreign or within species) DNA which may be removed before regulatory submission [21]. Countries without biosafety regulations but that are planning or have already started utilizing gene editing technologies in the development of new crop varieties, must still decide which regulatory pathway to pursue. Regardless, domestic and international biosafety regulations – including those that regulate agricultural trade – will continue to struggle with appropriate processes for risk assessment of GM crops. The inclusion of GEd crops in the mix will likely further confound defining appropriate regulatory processes and the search for best practices in different jurisdictions. This has translated into different approaches and frameworks to the regulation of the most advanced and new plant breeding techniques.

The European Commission's Group of Chief Science Advisors [25] recommended that to ensure continued investment in innovative plant breeding within the EU, the EU's GMO Directives required significant revisions to better reflect breeding technologies. This includes regulating GEd crops as conventionally developed varieties. The EU's current approach to GM crops contrasts with the science-based regulatory approaches in several countries in the Americas and Australia, which appear to be the most conducive for innovation investment. For example, one outcome resulting from the current degree of uncertainty in the EU has been in firms reducing their research and development investments there [60]. As more GM and the subset of GEd crops that may be regulated are being researched, developed, and transferred to farmers globally, the need to define feasible regulatory approaches grows. If all or a subset of the GEd crop portfolio are regulated as GM crops in a jurisdiction, they will endure the same regulatory fate as GM crops in those jurisdictions. The implication of this outcome is the need to understand the regulatory context and landscape in which GM crops operate to better understand the GEd crop regulatory landscape and enabling environment.

GM crops have been a quite successful innovation. The International Service for the Acquisition of Agri-biotech Applications [35] reports that around 14 percent of world crop areas are now GM, with more GM crops grown in developing countries than developed countries. Seventy-one countries now grow or import GM crops, but domestic biosafety regulations continue to diverge. Country divergence related to the inclusion of socio-economic considerations (SECs) in GM regulations has been, to date, particularly contentious. SEC inclusion in biosafety regulation is allowed, although not mandatory, under Article 26 of the Cartagena Protocol on Biosafety (CPB) for the assessment and approval process to import, research, or commercially produce a GM crop. The CPB, an implementing agreement of the Convention on Biological Diversity (CBD), establishes the rights of recipient countries to be notified of and to approve or reject the domestic import or use of living modified organisms. Those decisions are to be made using a biosafety assessment and a decision-making process. While most countries utilize the globally accepted science-based risk assessment methodology developed via the efforts of the Organisation for Economic Cooperation and Development, the potential to include frequently ill-defined SECs, creates uncertainties and thus, may introduce delays in the approval of GM crop varieties [43, 28].

Many developing countires lacked biosafety regualtory frameworks prior to the creation of the CPB. As biosafety acts and regulations were developed, many African and Asian countries that had colonial ties to the EU turned to the EU for guidance in the development of their biosafety frameworks [51]. There were many areas of influence in the EU overarching positions that caused challenges for developing country implantation of biosafety regulations. EU guidance was provided for numerous key CPB aspects in addition to SECs that included, among others: risk assessment, risk management, commodity export and international shipping documentation requirements, and liability and redress mechanisms. Additionally, any country wanting EU preferential tariff rates for agricultural exports, as allowed by the World Trade Organization, was required by the EU to ratify the CPB to receive the lower tariff rates [26]. The result for most developing countries that had strong historic trade with the EU was that they had no choice on whether to adopt the CPB; they were forced by practical considerations to do so. For many developing countries, the EU represents their key commodity export market, and therefore, the EU's rejection of GM technologies heavily influenced the development of their biosafety frameworks. This also meant that many developing countries made SEC assessments a mandatory part of their biosafety frameworks, perhaps reflecting the requirements of some European nations (such as Norway and the Netherlands) which, as explained below, require applicants to address certain SEC factors and specific issues in the assessment process. The challenge this inclusion of SEC assessment in the regulatory process has created for these countries is that, in many instances, no method for assessing SEC factors existed, which created barriers for the commercialization of GM crops given that the required SEC assessment could not be undertaken or could not be undertaken in a timely manner.

Developing the conceptual framework and operational instruments for SEC assessment as it relates to the regulatory approval of GM crops is still ongoing. However, considerable uncertainty regarding factors, methods, processes, data, and quantification continues [42]. As the CPB Parties expressed the desire and need to achieve conceptual clarity related to SECs to devise their own biosafety regulatory systems and/or meet their international obligations, they commissioned an Ad Hoc Technical Expert Group (AHTEG). The AHTEG on Socio-Economic Considerations of the CPB Conference of the Parties is to help elucidate SECs in relation to the CPB and

biosafety regulations and achieve conceptual clarity related to SECs. It has prepared a draft 'Guidance on the Assessment of Socio-Economic Considerations in the Context of Article 26 of the Cartagena Protocol on Biosafety'. The Guidance Document defines SECs in this context as 'economic, social, cultural/traditional/religious/ethical aspects, as well as ecological and health-related aspects' provided they are not already covered by risk assessment procedures under Article 15 of the Protocol. This definition, considered also by Ludlow [43], recognizes that the meaning of SECs are highly dependent on regional and national circumstances. The Guidance Document focuses on the processes for conducting SEC assessments and is due for further consideration at COP/MOP 10, now scheduled for 2021.

Conceptual clarity around SEC assessment is needed for effective regulation and enhancement of investment in plant breeding technologies such as GM and gene editing [29, 66]. In general, achieving conceptual clarity means the ability to understand the concept itself, understand the reason for its existence, and understand the processes involved in its implementation. Conceptual clarity implies that concepts can be explained in such a way that it is simple enough for any stakeholder to relate to it in simple terms and is important for ensuring that all stakeholders define and interpret terms in the same way.

As noted above, the AHTEG was tasked with preparing a document to improve conceptual clarity regarding the SEC methods available, the protocols for their application, and necessary data requirements. This happened because Parties were expressing that their regulatory systems had a significant lack of clarity surrounding SECs and their relationship to their domestic regulatory processes, which in some cases mandate SEC inclusion in decision making. In some countries (both CPB signatories and non-signatories), integrating SECs into domestic biosafety assessments, the lack of clarity on which factors to assess, how to assess them, and what methodologies could be applied to complete the analysis, regulators are limited in their ability to undertake and complete SEC assessments. These uncertainties result in the products undergoing assessment becoming stalled in the regulatory approval phase of the innovation pipeline. To increase the efficiency of SEC assessment, the AHTEG reviewed existing applications and processes, reporting back with information and insights that would improve the conceptual clarity of SEC assessments [15]. This had limited success due to the very limited country response on the utilization of SECs in domestic biosafety regulations.

This article seeks to address some of these deficiencies. It proposes categorizing SEC assessments into three groups based on the methodological approaches commonly used to conduct them. These are empirically based, legally grounded, and consensus approaches. The article focuses on, and updates the application of, SEC assessment in the approval of GM crops. The discussions in this article will inform the conceptual clarity-seeking process for those nations requiring SEC assessment of GM crop varieties. The article concludes with a discussion of the potential impacts of applying SECs to the regulation of gene editing technologies if GEd crops are subjected to GM crop regulations and especially to SEC assessment requirements.

2. SEC Factors

Theoretical frameworks have been developed for socio-economic assessment of GM crops. One such framework has been developed by the European Commission [25], proposing nearly 100 different factors that can be used to assess GM crop adoption impacts for technology developers, farmers, food processors and consumers. The lack of GM commercialization within the EU has resulted in this framework never being applied. Additionally, Argentina and Brazil utilize market and trade analysis as part of their approval process for GM crops. Two aspects of this analysis are of crucial importance. The first is that the process for this analysis is clearly defined in terms of scope, approach, implementation, and decision making rules. The second is a matter of process, sequence, and coordination with the risk assessment process. Taken together, these two aspects allow both countries to conduct effective and efficient SEC assessments that do not indeterminately delay the regulatory approval process.

The book by Ludlow et al. [43] provided expert commentary on the assessment of 15 different SEC factors. These factors were determined following consultation of various CPB and related documents discussing SECs. While a debate about narrow versus broad application of SEC factors exists, the methodological review was purposively designed as broad, thereby providing information to countries that may include SEC assessment in their domestic regulatory framework that differs from a narrowly constructed list.

Factor experts were requested to assess their factor through a template that was applied to all 15 factors. The template required information on methodologies available to undertake a SEC assessment, a critical assessment of what data would be needed and where data gaps existed, what international obligations exist that require compliance, and what domestic administration coordination might be required.

We propose that the 15 factors considered by Ludlow et al. [43] can be grouped into three methodological categories: empirically based, legally grounded, and consensus approaches. These groupings are used below, to discuss developments in SEC assessment.

3. Empirically Based Methodologies

Empirically based methodologies respond to questions raised mostly in the economics and social sciences realm. SEC factors that use empirically based methodologies for assessment include adoption and use impacts on producers, consumers, international and national trade, as well as consumer choice [43]. Other realms that may be evaluated using empirically based methodologies include environment, biodiversity, and health, which may have a social and economic component attached to their impact [43].

Multiple empirically based methodologies have been used to assess such factors that have advantages and disadvantages,

varying data requirements and data gaps, as well as complex implementation contexts, which may limit the relevance of the results for other countries or other crops. For some SEC factors, there are de facto standards that implementing organizations must adhere to, including Codex Alimentarius for food safety assessments, the Organisation for Economic Cooperation and Development (OECD) Blue Book, and the Food and Agriculture Organization of the United Nations (FAO) guidance on environmental assessments [42]. However, for the most part, the lack of such internationally-validated standards for SEC assessment implies that assessment practitioners are encouraged to apply elements of best practice to ensure high-quality research and method implementation [59].

A rich tradition of examining the impacts of technology adoption on producers, households, and society exists [44, 46, 57, 52]. Methods available for implementation are mature, although relatively few are used. These include methods in economics and social sciences, which are typically applied before or after technology adoption. Applied methods measure costs and benefits incurred, actor roles and relationships, and the conditions by which gains are ascertained and distributed among actors. In general, available literature shows positive gains from the adoption of GM crops, but wide variation exists across actors, crops, traits, regions, and over time [62, 35, 49, 37].

In contrast, methods used to examine consumer choices are still evolving. These methods consider stated (what consumers say they do) versus revealed (what consumers do) preferences, which use price information and other factors to explain consumer behavior. Existing methods of this type rely on the assumption that consumers are rational and thus their choices are rational [16, 2, 45]. Stated preference using consumer's willingness to pay is typically used in evaluating environmental and biodiversity conservation efforts. However, both stated and revealed preference approaches have limitations that somewhat restrict their applicability. Stated preference relies on people's hypothetical choices in an experimental context. Respondents can choose the 'best' alternative from a hypothetical portfolio of scenarios identified in the experiment's design. This approach provides for the opportunity to assess potential new policies, non-observable activities or situations where multiple attributes describing the issue under assessment may exist. The main limitation of stated preference methods is the potential for strategic behaviors and responses, and the possibility of not being able to include behavioral constraints that may affect decisions. In turn, by relying on observable choices, assessments using revealed preference approaches are largely limited to observable states of the world. This implies that these methods may not be suitable for assessing preferences for attributes that cannot be observed directly or where no variation exists. Substantive expertise is needed to examine consumer issues, especially in developing economies where market prices may be non-existent, where prices may not be reflective of full value to consumers, and households' preferences such as in subsistence economies where food security is a concern and where significant limitations exist to characterizing consumers and their behaviors.

Methodologies examining biodiversity require further refinement, particularly regarding ecosystem services. Methods pursued to date examining biodiversity and ecosystem services have advantages and disadvantages that need careful evaluation, particularly when supporting decision making. Such methods can be grouped into three major categories, including the use of biodiversity indicators, measure of taxonomic diversity, and those that attempt to estimate an economic value to taxonomic diversity. Biodiversity indicators and measures of taxonomic diversity have been described in Smale [58], Millennium Ecosystem Assessment [47] and Biodiversity Indicator Partnership [19]. These are approaches that are evolving and maturing pending further developments in addressing methodological issues related to measurements.

The economic value of taxonomic diversity may use monetary or non-monetary terms, and includes tangible and intangible values. Methods include those using stated and revealed preference, cost based, and system approaches. Limitations of stated and revealed approaches have been discussed previously. Cost-based approaches may have limited applicability where no market exists or where prices do not reflect full value to society. System approaches are still relatively immature and may be more difficult to implement as they merge indicators and different approaches to measure value.

A more critical limitation is that results using all biodiversity assessments may not be extrapolated to estimate value in other ecosystems, may be specific to the observed population, and may be relevant for a particular point in time, and addressing non-use value such as those related to cultural, religious, ethical and/or aesthetic value may be difficult, but their exclusion may underestimate the true value of biodiversity and ecosystems services. The relatively immature state of methodologies means expert support and implementation capacity is required. Needs exist to continue advancing methods and to explore innovative approaches that will fill data gaps in developing economies [6].

Environmental impact data have shown positive outcomes resulting from GM crop production [8, 49, 37], including reductions in pesticide use and greenhouse gas emissions. Other issues such as pest resistance management, secondary pest emergence, and the impact of herbicide bans and delays in pesticide resistant traits have also been studied [71, 9]. A major lesson to date for environmental assessments is the need to define the proper counterfactual or comparator by which to evaluate the GM crop interventions [7]. All agriculture impacts the environment and comparisons with second-best alternatives are needed. Furthermore, broad environmental assessments need to account for reversible and irreversible impacts, while addressing explicitly private versus external benefits and costs.

Methodologies used to evaluate bilateral and multilateral trade are quite mature. Analytical approaches incorporate static and dynamic approaches examining individual production systems and crops [32, 3, 65]. Models typically used in these approaches take advantage of existing trade databases maintained by various organizations such as the Global Trade Analysis Project, World Trade Organization (WTO), and the World Bank. Existing models may consider impacts at the national, regional, and/or global level. Countries themselves are usually

interested in examining national trade interests, as GM crops may induce negative externalities due to adoption. Market risk may be relatively significant, yet manageable. Such national trade impacts need careful evaluation on a case-by-case basis to determine how real potential market risks are in practice.

An element of best practice in conducting a national trade assessment is to conduct a basic market analysis done as an initial and rapid consultation to identify potential market risks (if any) and, more importantly, identify potential management strategies for implementation. This approach was pursued by Gruère [34], which ensures identification of any potential issue and, if there is no relevant issue, avoids conducting a more involved assessment. Even a basic market analysis requires substantial expertise to examine market and regulatory data, usually on a case-by-case basis. An important aspect to consider is that decisions to reject GM products for import, although compatible with the CPB, may violate WTO standards [36]. Special care is needed in those instances where management options are feasible and/or cost efficient, and in which case an economic assessment should describe these and be considered along with the potential trade issues for inclusion in decision making. The focus should not be only on risk or hazard identification, but also on describing management and mitigation strategies.

Multiple approaches and methodologies are increasingly being used to examine food security issues [54, 1]. This is a result of the understanding that food security is a complex issue requiring multiple approaches for its assessment. Understanding food security implications is an important task, especially in developing countries. Thus, special care is needed to ensure proper assessment where relevant. From the standpoint of supporting decision making, food security assessments may be relevant to examining the overall impact of technology innovations rather than specific technologies considered for deployment. Food security assessments may also be time-intensive and protracted exercises and not compatible with time-limited decision-making processes required for biosafety regulation.

4. Legally Grounded Methodologies

Legally grounded methodologies require the collection and interpretation of relevant normative documents and policy developments. Such methodologies are pertinent to multiple SECs and there is growing awareness of the impact of developments in one international regime on other regimes [5]. Developments around genetic resources and the associated digital sequence information is an example [61]. Such resources and information are important to development of GM and are particular flashpoints for two SEC factors: traditional knowledge (TK) and intellectual property (IP).

The most significant recent development in the CBD regime relevant to genetic resources and associated digital sequence information is the creation of the post-2020 Global Biodiversity Framework for COP 15, now scheduled for 2021. Given that the CPB is part of the CBD regime and that it is in that forum that future negotiations and developments will occur, negotiations to include genetic resources within the Framework's scope are particularly important. The Nagoya Protocol, which requires compliance with access and benefit-sharing (ABS) obligations for genetic resources and associated TK, is another important part of the CBD regime [38]. This regime recognizes that digital sequence information on genetic resources is included by some countries as part of their ABS frameworks, although there is strong divergence in countries' attitude to this.

The World Intellectual Property Organization (WIPO), which administers the world's IP conventions, is developing international instruments to protect TK, including genetic resources, through its Intergovernmental Committee on IP and Genetic Resources, TK and Folklore [69]. Mandatory disclosure of origin regarding patented inventions using genetic resources is a significant area of contestation here. In parallel, negotiations on a draft Design Law Treaty by the WIPO Standing Committee on the Law of Trademarks, Industrial Designs and Geographical Indications have seen the African Group countries seek the option for countries to require disclosure of origin in industrial design regulations. Finally, the Governing Body for the International Treaty on Plant Genetic Resources for Food and Agriculture is undertaking international discussions relevant to IP and TK on this issue, but has not resolved whether digital sequence information should be included within the Treaty's scope [4, 22].

Regardless of the SEC, legally grounded methodology requires knowledge of the assessing country's obligations under multi- and bilateral agreements relevant to the SEC and assessment by those trained in interpretation of legal and policy documents. This methodology also requires an understanding of the context and real-life responses to the relevant documents. For example, accurate assessment of the SEC factor of IP or the implications of IP for other SECs such as ethics, requires knowledge of the real IP landscape for that application. In the context of GEd crops, the owners of much of the IP in the technology have declared that they will provide broad access through non-exclusive licenses for use in commercial and academic agricultural research and product development [55]. Further, the joint license adheres to ethical restrictions for agricultural use, which prohibit using CRISPR for gene drive, sterile seeds, or tobacco products for human use.

5. Consensus Approach Methodologies

Consensus methodologies are the most challenging of the methodological categories, as they focus on attitudes and perceptions. Consensus approach methodologies are commonly used to examine SEC factors such as labor, ethics, culture, and religion [33, 67, 23, 30]. The challenges of engaging subjective measures of assessment for questions like 'Is this the right thing to do?', are many and include that the response from food secure countries can be the opposite of food insecure countries. The lack of science- or evidence-based measures also commonly leads to the polarization of discussions.

While data are not gathered in the sense of empirically based methods, public engagement events are organized and held, that provide responses for consensus method evaluation. Consensus approach methodologies are designed to ensure

agreement on the resulting outcomes or recommendations, and as such can be held hostage by individual participants with an ulterior motive that refuses to agree with any recommendation that a GM crop be approved. Acceptance of new technologies is correlated to the ability to access accurate information [56], creating challenges for the demographic makeup of citizen panels. The challenge of consensus-style methods and their inability to provide clarity or resolution is perhaps no better illustrated than by the failure of WIPO and the Treaty on Plant Genetic Resources for Food and Agriculture to reach agreement on a definition for digital sequence information, despite over a decade worth of consultation, dialogue, and meetings [61].

A further challenge for consensus approach SEC factors is the level of participant knowledge prior to participating in a public forum. For the facilitation of informed discussion, a defined level of pre-existing knowledge is required. However, public participation forums can encourage the participation of individuals that self-identify as possessing little to no knowledge of the subject matter. The impact of such participant inclusion is that decisions may be based on erroneous or false information.

6. Lessons from Including SEC Assessment in GM Crop Regulations

In December 2019, a meeting of the SEC AHTEG was held in Vienna, Austria. The objective of the meeting was to gain context and principles supporting conceptual clarity regarding the application of SECs in domestic biosafety regulations. Parties were invited by the Secretariat to make submissions on "(i) preliminary experiences using the voluntary Guidance, as well as (ii) examples of methodologies and applications of socio-economic considerations, in the light of the elements of the voluntary Guidance, preferably in the form of case studies..." [10]. The SEC AHTEG meeting report indicates submissions were limited, with few submissions reporting on SEC methodologies that had been applied and what the outcomes and results of application had been [18].

As the AHTEG report indicates, very few of the submissions provided examples that contribute to increasing conceptual clarity. Nevertheless, the minority of submissions provide some insights. The French submission suggested that cost-benefit analysis is sometimes capable of assessing social factors [11]. The submission goes on to say that identification and quantification of benefits and risk should preferably be done in monetary terms. Norway's submission identified that SEC assessment had contributed to the rejection of several GM canola varieties [12]. The Norwegian Ministry of the Environment conducted SEC assessments, identifying that, "some Norwegians have expressed ethical concerns about the use of GMOs". Norway does not have a defined ethical assessment framework, and the submission appears to indicate that individual or organization expressions of concern carry considerable weight. A report on formalizing assessment of ethical concerns has since been reported to have been prepared for the Norwegian Ministry, but whether it is adopted or not, decision making will remain a matter of subjective deliberation [48]. Nigeria's submission provides an insightful methodological perspective in that greater consideration is given to SECs that are science- and/or evidence-based [13]. South Africa's approach to inclusion of SECs in biosafety assessment is perhaps the most straightforward of the nations including SECs in regulatory approval. Approval decisions are made by the Executive Council and if it is ruled that the approval of a GM crop will not pose adverse effects on humans or any socio-economic impacts, then no SEC assessments are conducted [14].

The report goes on to indicate that more time may be needed to allow for Parties to use the existing Guidance Documents. To supplement the experience paucity on the assessment and inclusion of SECs into decision making, we have identified the existing experience of SEC assessments that are beginning to develop and from which we draw the following preliminary lessons, based on our consultation of the literature and documentation submitted to the SEC AHTEG and the CPB Biosafety Clearinghouse.

6.1. Preliminary assessment

Responding to the CPB Parties' request to the SEC AHTEG and to SEC experts, to achieve conceptual clarity we propose an initial step that is helpful for the potential implementation of SEC assessments. For countries to achieve conceptual clarity on inclusion of SECs into regulatory processes, they need first to clearly articulate why they want to include SECs and whether inclusion improves society's welfare. Furthermore, countries need to be aware of the additional regulatory burden and innovation delays derived from their inclusion. This implies careful evaluation of benefits, costs, risks, and outcomes/implications from such inclusion. This exercise may be helpful even in those situations where national regulations already include SEC assessment as a mandated step for informing decision making. The rationale behind conducting this exercise is to help identify the more relevant SEC issues to decision makers and to rank those according to importance. This exercise may need to be repeated as SEC issues may vary across crops, traits, and locations, yet these future discussions need to be pragmatic and ideally the product of initial conversations between proponents, regulators, and decision makers. These preliminary discussions may help avoid protracted and unnecessary SEC assessments. An example of such process already being used is that taken in regulating GEd plants in Argentina [40].

6.2. Scope

SEC assessments are most efficient when consistent and coordinated with the implementation of environmental risk assessment approaches. In the case of South Africa, for example, an important objective of environmental risk assessments is to identify those events with negative impacts. Projects with negative impacts will not be approved for environmental release. Therefore, a SEC assessment is not required because it will not overturn a negative environmental impact. Projects with no negative environmental impacts on the other hand, may undergo a SEC assessment, which is defined by the competent domestic

authority. SEC assessment efforts should also be proportional to expected SEC impact, as is the case with environmental risk assessments. For example, a project that will be contained (e.g., plants as bioreactors for pharmaceuticals) is unlikely to have a negative SEC impact because the plant is not likely to enter the food/feed value chains. A SEC assessment should therefore not be required or should be limited in scope.

This approach contrasts with that pursued in Kenya, which is built from the bottom up through stakeholder consultations. Standard operating procedures developed by the competent regulatory agency include guidance questions about the type of factors for inclusion, but no guidance on methods or evidence, nor do they provide a benchmark or standard to guide decision making. Information on SECs provided by the applicant are sent for anonymous peer review, which decide the correctness of data and evaluation process, but also if the submitted information is sufficiently convincing. A practical limitation is that there is no guidance on how to weigh the evidence provided to decide on its robustness. An example of established regulations includes those of the Netherlands [17], which has established SEC categories and quantifiable indicators. Another example is that of Norway [50], which has delineated a set of SEC factor and specific issues/questions that need to be responded to by applicants. These focus on sustainability, benefits, ethical issues, and other SEC factors.

The disadvantage of defining the universe of SEC factors and specific questions in advance, as is the case of the Netherlands and Norway, relates to the specific crop, trait, and regulatory stage of development. Some SEC factors or specific questions may not be relevant for a specific application, and if the guiding regulations do not clearly include flexibility to use available literature, experience from other countries and/or allow the possibility of answering 'does not apply', this may cause unnecessary, and in some cases redundant, efforts to respond to a required question/issue. For example, if national regulations require a SEC assessment at the laboratory and/or confined field trials or even multi-locational trials stage, the SEC assessment may be redundant as the technology may not advance to a subsequent stage due to technical reasons. Thus, the need exists to encourage regulators and decision makers to consider SECs only at the last stage for commercialization or deliberate release. Alternatively, limiting the scope of the potential issues and questions for earlier stages provides the flexibility to answer questions/issues in a feasible and efficient manner.

6.3. Methodology

Methodological choice depends on which SEC factors are to be assessed. Many SEC factors of potential concern are likely to be specific to the GM crop, trait, and place of intended release. The methods to be chosen for implementation may also be dependent on those circumstances. As discussed above, some biodiversity impacts and ecosystems services may be site and time limited, thus extrapolation may be limited. In other cases, such as economic assessments measuring producer and consumer benefits, results may be contextualized. In these cases, the need exists on the one hand to ensure that comparisons and extrapolations are carefully done, but also for regulations to have the flexibility necessary to allow use of literature and data generated elsewhere.

The decision to implement a specific method, method mix or even to use data generated elsewhere is a technical one, preferably done by SEC experts with experience in SEC assessments. The recommended initial step described previously of having a preliminary conversation between regulators, developers, and policy makers to define potential SEC factors for evaluation and then for SEC assessment experts to choose methods that respond to those factors, can help avoid duplications and wasted time and resources in unnecessary SEC assessments.

A further important recommendation around methodology is to focus on the SEC evaluation process, including implementation, coordination, and decision-making standards. The approaches of Brazil and Argentina are examples here. In Argentina, there is a well-defined approach to assessments, with limited questions about SEC factors of relevance to Argentina and its decision-making processes. The process is mandatory and done by an agency within the Ministry of Agriculture. In contrast, the Brazilian process is not defined in advance, but instead responds to specific SEC factors identified during the risk assessment process. A decision-making body identifies SEC factors for further evaluation and then commissions a study to a third party. The information gathered is then used in the decision-making process.

A defined approach to SEC assessment needs to consider proper evidence, preferably using verified data and elements of best practice implementing methods for the evaluation of SECs. Use of scientific methods for SEC assessments are the preferred way to support policy and decision making, although implementation of SEC assessments is hampered by the lack of internationally-validated protocols for SEC assessments (such as CODEX or OECD for food/feed and environmental safety, respectively) to secure compliance with generally-accepted practices. A second alternative is for SEC experts to comply with a set of generally-accepted elements of best practice.

7. Implications for the Regulation of Gene-Edited Crops

Gene editing in crops is being quickly taken up and could revolutionize global agricultural productivity. Gene editing is particularly attractive to developing countries and public sector research and development because when compared with GM, gene editing may be more cost effective, faster in development, and may address productivity constraints and changing climatic conditions that have been previously intractable [53]. Some early estimates identify some of the cost advantages of using gene editing in crops and other organisms [31, 39]. However, these advantages – especially costs – may be partially predicated on regulatory authorities not subjecting them to the same regulatory regime as GM crops.

The application (or not) of GM regulations to GEd crops is still evolving. The European Union's Court of Justice, for example, decided in 2018 that gene editing falls within the EU's GM regulations, while other jurisdictions regulate only some

gene editing techniques as GM [21, 24]. As described previously, countries tend to regulate GEd crops as GM only if they contain foreign DNA and its insertion is permanent [40]. Lassoued [39] has estimated that if GEd crops are regulated as equivalent to GM crops, the additional regulatory burden is substantial, with an extra nine years and $14 million in regulatory costs required for each variety submission. These time and fiscal costs will be most prohibitive to public sector plant breeders attempting to develop and commercialize GEd varieties [66].

In contrast, several leading GM crop-adopting countries have clearly identified that a subset of crop varieties developed through gene editing will not require additional regulatory oversight, if no foreign DNA is present in the variety delivered to farmers. Regulatory agencies in Argentina, Australia, Brazil, and the USA have all indicated that GEd varieties with no permanent foreign DNA insertion will be treated in the same way as products of conventional plant breeding [21, 63]. Even GM crop-importing countries are beginning to clarify their policy positions regarding GEd crops, with, for example, the Japanese Consumer Affairs Agency confirming that GEd food products will not require risk assessments and that GM foods would and will enter the market without labels [70]. New Zealand has adopted a similar regulatory strategy to the EU, firmly articulating that all GEd crop varieties will be regulated as equivalent to GM crops [68]. In August 2019, the Council of the European Union requested the European Commission submit a study by April 2021 on the EU's options for addressing the challenges of trying to regulate GEd varieties using the existing regulatory system [20].

With leading agricultural producing nations indicating that crops created using some GEd technologies will be treated in the same way as those arising from conventional crop improvement methods, freeing these varieties from the additional regulatory oversight required for GM crop varieties, it is expected that significant research initiatives will engage gene editing tools. However, GEd crops may introduce new problems for trade if the current landscape, where some countries regulate these technologies as GM, persists. For example, an important regulatory implementation challenge created by GEd crops is that some are not easily distinguishable from plants created by other forms of mutation. GM crops have marker genes inserted along with the desired trait, such as herbicide tolerance or insect resistance, meaning that simple assay tests can detect the marker gene and regulators or importers can detect whether a GM crop is present. However, in those cases where no permanent foreign DNA exist or persist, GEd varieties can be indistinguishable from results of other forms of mutation. The challenge this creates for process-based regulatory systems, such as the EU's regulatory system, is that there is no ability, or at best, very limited ability, to detect at the port of entry if a shipment contains a GEd crop variety or whether a new variety is GEd. This introduces the possibility that the EU will require certification providing a guarantee that a shipment or a variety is not GEd. More importantly, the EU's regulatory system has a scant approval record regarding GM crop varieties. Only a single variety has been approved since 2003. If such an approach is taken by the EU to GEd crops, plant breeding's move from GM to GEd offers no solutions, and instead further compounds existing problems and challenges.

Whether a GEd crop is considered as a GM crop or not in national biosafety processes, such processes must be practical if agricultural innovations are to reach their potential. SEC assessment should contribute to the regulatory process and not be used as a barrier to commercialization. SEC assessment has its own costs and difficulties, which add to the time and costs of the approval process. If SEC assessment is required by a national biosafety regime, it is best undertaken in tandem or preferably after the biosafety risk assessment has been completed, to minimize costs associated with SEC assessments. Regardless of whether these costs are great or not and who they are borne by, this avoids wasting resources preparing for and/or conducting SEC assessments that will not be needed.

There is growing consensus among experts, with which we concur, that if no foreign DNA is permanently present when the product reaches farmers, the organism is not GM and is not within the scope of the CPB. However, some countries apply national biosafety measures to GEd crops in the case where there is permanent integration of foreign r-DNA. Whether GEd crops that are deemed to be conventional crops are within the CPB's scope and, if so, guidance on risk assessment, are further challenges for the COP/MOP 10 [18]. The SEC assessments of potential benefits to producers, consumer, and society focused on economics, for GEd crops, will be dependent – as with any other agricultural technology – on the investment costs necessary to bring the technology to producers. The research and development and regulatory costs are therefore a key determinant in defining the value of GEd crops to society. This bolsters our argument that if any specific GEd crop technology under consideration is regulated as GM, then it is unlikely that it will reach producers, as investment in such technologies introduces an element of uncertainty and risk to developers, especially in the public sector. We hope that policy makers, especially in developing countries, will take this conclusion into consideration when defining inclusion of SEC assessments and GEd crops in their deliberations.

8. Conclusion

The taking into account of SECs in authorization procedures is, in general, unfeasible since there is no generally-recognized methodology of how to carry out a SEC assessment. Therefore, the outcome of any such assessment is unpredictable. The degree of uncertainty resulting from the inclusion of SEC assessments as part of the approval process for GM crops creates a barrier to the commercialization of these products. This is due to the cost and effort involved, but most importantly, through the introduction of risk and uncertainty into the investment decision process. One potential solution for GEd crops could be that SEC assessments be conducted only in those situations where a negative impact may occur. Proportionality between the level of SEC scrutiny and expected impact should be a guiding principle for policy development and implementation. If it is decided to implement

SEC assessment as part of a regulatory process for GEd crops, that decision should be tied to the decision to regulate a GEd crop as a GM crop, and a differential approach to assessing SECs should be taken that defines and focuses on what is different about a GEd crop compared to a conventionally-bred crop.

9. References

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