LEEWAY TO OPERATE WITH PLANT GENETIC RESOURCES

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LEEWAY TO OPERATE WITH PLANT GENETIC RESOURCES

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EDITORIAL
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Editorial: Leeway to Operate With Plant Genetic Resources

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Keywords: access and benefit-sharing, biosafety, intellectual property, plant genetic resources, research and breeding

Editorial on the Research Topic

Leeway to Operate With Plant Genetic Resources

Different legal frameworks are applicable to the use of genetic resources (GR). These can broadly be categorized into (1) access and benefit-sharing (ABS), (2) biosafety aspects related to the technologies for improving the genetic material, and (3) intellectual property (IP) systems including plant variety rights (PVR) and patents specific to the plant innovation sector. With scientific and technical progress in research and breeding, as well as expanding internationalization, legal frameworks have become increasingly complex in the past few decades. In this context, the Research Topic "Leeway to operate with plant genetic resources" addresses the latest and most pertinent legal issues related to the use of GR in plant research and breeding. The contributions are summarized here and put into the larger societal and legal context that modern-day plant geneticists are facing.

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ACCESS AND BENEFIT-SHARING

ABS is a framework that aims to distribute fairly the benefits arising from the utilization of GR between users and providers. The basic principles are drawn in the Convention on Biological Diversity (CBD) and its supplementary protocol, the Nagoya Protocol (https://cbd.int/abs/). The access to GR also considers the related traditional knowledge and is based on prior informed consent and mutually agreed terms.

There is a wide disparity in how the Nagoya Protocol is implemented in different countries, which is challenging for users. Sirakaya et al. reviews the ABS framework across 20 provider countries, identifying common regulatory elements and follows up with stakeholder interviews. These show that opinions on the benefits of various ABS regulatory mechanisms differ between provider countries and industrial users, though there are some common grounds. One significant detail is that most users oppose the inclusion of digital sequence information (DSI) within the subject matter, contrary to most provider countries. We note that FAO acknowledges that DSI increases the understanding of molecular biology and evolution as well as taxonomy and identifying species, thus facilitating GR conservation and use. Aubry et al. elaborates further on the ongoing debate about the sharing and mining of freely accessible sequencing data. In his view, DSI of plant genetic resources for food and agriculture (PGRFA) should be under an "*efficient, resilient, decentralized*" and reasonable governance model that ensures its fair use.

Brink and van Hintum address the perspective of collection holders, showing the challenges faced by gene banks for acquiring and sharing GR while complying with the various international and national regulations. They argue that gene banks must set up appropriate protocols for

documenting every accession's origin and the condition for its use and further distribution, while countering complexity to avoid a decrease in access to PGRFA. Overall, it is important to ensure fair and equitable ABS negotiations between providers and users. Deplazes-Zemp et al. brings an ethical perspective, arguing that there are five types of justice related to this subject: distributive, commentative, recognitive, reparative, and procedural. According to the author, it is important that both users and providers are aware of these justice types and the way the use of GR poses particular challenges.

BIOSAFETY

The products of gene technologies, such as genetically modified organisms (GMOs) are subject to a specific biosafety legislation, in most jurisdictions. building on principles established by the Cartagena Protocol to the CBD (https://bch.cbd.int/protocol/). The legal status of the products of new breeding techniques (NBTs) has been subject to many discussions, as the resulting products may or may not be encompassed by the GMO definition, depending on the jurisdiction.

A landmark judgment from the Court of Justice of the European Union (CJEU) in July 2018 (case C-528/16) means that the products of site-directed mutagenesis will be subject to the same legal provisions as genetically modified organisms (GMOs). There are however discussions on the applicability of the CJEU judgment to the variety of NBT products. Vives-Vallés and Collonnier provide a legal interpretation of the judgment, relating it to relevant scientific papers published in the aftermath. Their article concludes that certain products of NBTs may be exempted from the scope of Directive 2001/18/EC, despite the CJEU judgment being commonly interpreted otherwise, and sketches a limited legislative proposal to achieve certainty and suggesting which NBT products could be exempted and under what circumstances. Holme et al. argues that the CJEU assumption that targeted mutagenesis "*makes it possible to produce GM varieties at a rate and in quantities unlike those resulting from random mutagenesis,*" is incorrect. Technical developments including TILLING has led to a convergence between the two types of mutagenesis in terms of output, with the main differences being the precision of mutation site and the number of off-target mutations.

Turning to the economics of regulating NBT products, Wesseler et al. compares theoretical advantages and disadvantages with different regulatory approaches. A survey among Dutch plant breeding companies show that these are optimistic the prospect that a more relaxed legislation will be implemented in the EU, despite having experienced a negative impact on competitiveness and on investments due to the CJEU judgment on mutagenesis. Jin et al. present an example of costs in delaying technology adoption. By assessing the impact caused by postponed authorization for the use of *Bt* rice in China, the authors model the costs by filling an information gap regarding foregone benefits of lower pesticide use and the spill-over effect by delaying technology adoption. They conclude that delaying *Bt* rice introduction has come at a substantial economic cost (both direct as well as in terms of human health and environmental costs).

The Green Revolution based on crop genetics along with advanced agronomy led to miraculous harvests in Asia and Latin America, but largely bypassed sub-Saharan Africa. The ongoing gene revolution should therefore bring benefits to this region. Komen et al. show how the authorization of transgenic crops release is managed, drawing examples from five African countries. They highlight challenges and lessons learnt and propose policy recommendations facilitating the adoption of emerging biotechnology for plant breeding in Africa. It has however been recognized elsewhere in the literature that the global influence of EU policies should be considered. The overall process for risk assessment and risk management of GMOs in the EU has been criticized as being unnecessary politicized and, though the part with the science-based system for risk assessment is overall sound, certain improvements are envisaged by Chatzopoulou et al.. The authors compare the procedure in the European Food Safety Authority (EFSA) with that of the European Medicines Agency (EMA), and suggest that a more balanced geographical distribution of experts in the EFSA GMO panel may minimize overall politicization of decision-making.

INTELLECTUAL PROPERTY

Current technical developments are posing challenges to the IP/PVR systems in plant breeding. Definitions need to be re-established and the impact of the evolution of systems for patents and for plant breeders' rights need to be analyzed in terms of market structure and competition. One example is the concept of Essentially Derived Variety (EDV), for which UPOV is currently revisiting their explanatory note. Krieger et al. explore the concept and assess whether the use of NBTs invariably leads to an EDV. The authors deliver a legal interpretation of two related notions, namely, the "breeder's exemption" and EDV, considering the wording of the provisions, the historical background and the evolution, including also assertions from case law from several UPOV members. Several elements are discussed, concluding that the EDV concept should encompass cultivars obtained through the application of NBT only, when no further significant breeding steps have been taken.

In terms of market structure and innovation, Wozniak et al. analyse the current situation and prospects of rapeseed in the EU taking Poland and Germany as benchmarks. The study considers several IP as well as agronomic factors and analyses their evolution overtime, describing patterns regarding the opportunities of rapeseed. Though an analysis of IP shows an innovation potential, the authors are concerned that the CJEU judgment on mutagenesis may have a negative impact on the expansion of rapeseed cultivation.

Following concerns about the increasing impact of patenting and of concentration in the seed sector, an Open Source Seed (OSS) model has been proposed in recent years. Louwaars et al. investigates this model and its impact on the breeder's exemption specifically and on the open innovation character of the PVR

system in general. Focusing on two examples from Germany and USA, the author suggests that OSS models add additional pressure on the breeder's exemption, which may already be restrained by patents and biodiversity schemes, thus concluding that the breeder's exemption is an appropriate solution to ensure the access to genetic material.

Altogether, these articles illustrate the complexity of legal frameworks that plant researchers and breeders need to be aware of and comply with. Scientific and technological progress is enhancing our capacity to work with GR and causes restructuring of markets and competition and re-definitions of established concepts. We hope this Research Topic will provide a valuable resource for all stakeholders, including scientists, legal researchers, and practitioners that wish to stay up to date in this field.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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POLICY AND PRACTICE REVIEWS
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The Future of Digital Sequence Information for Plant Genetic Resources for Food and Agriculture

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The recent debates on the legal status of "digital sequence information" (DSI) at the international level could have extensive consequences for the future of agriculture and food security. A large majority of recent advances in biology, medicine, or agriculture were achieved by sharing and mining of freely accessible sequencing data. It is most probably because of the tremendous success of modern genomics and advances of synthetic biology that concerns were raised about possible fair and equitable ways of sharing data. The DSI concept is relatively new, and all concerned parties agreed upon the need for a clear definition. For example, the extent to which DSI understanding is limited only to genetic sequence data has to be clarified. In this paper, I focus on a subset of DSI essential to humankind: the DSI originating from plant genetic resources for food and agriculture (PGRFA). Two international agreements shape the conservation and use of plant genetic resources: the Convention on Biodiversity and the International Treaty for Plant Genetic Resources for Food and Agriculture. In an attempt to mobilize DSI users and producers involved in research, breeding, and conservation, I describe here how the increasing amount of genomic data, information, and studies interact with the existing legal framework at the global level. Using possible scenarios, I will emphasize the complexity of the issues surrounding DSI for PGRFA and propose potential ways forward for developing an inclusive governance and fair use of these genetic resources.

Keywords: plant genetic resources, digital sequence information, International Treaty for Plant Genetic Resources for Food and Agriculture of the Food and Agriculture Organisation, digitization, plant genetic resources for food and agriculture

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INTRODUCTION

In his Discourse of Inequality, Rousseau states: "You're lost, if you forget that the fruits of Earth belong equally to all of us, and Earth itself to nobody" (Rousseau, 1755). Similar thoughts were surely some of the underlying motivations of negotiators during the development of the International Treaty on Plant Genetic Resources for Food and Agriculture (PGRFA) in the early 2000, later referred here as the "Seed Treaty" (Esquinas-Alcazar et al., 2013; ITPGRFA, 2004). Since more than a century, the concept of genetic resources frames breeding and conservation into a genocentric perspective that is intertwined with their own erosion and the danger of losing biodiversity (Bonneuil, 2019; Harlan, 1975). As "fruits of the Earth" are becoming scarce in quantity and quality (Esquinas-Alcázar, 2005; Khoury et al., 2014), there is more than ever a need for fair and equitable governance of genetic resources, especially

those relevant for breeding new crops and food security (Genetic Resources for Food and Agriculture, GRFA).

Two international agreements shape the conservation and use of PGRFA: the Convention of Biodiversity (CBD) that rules any terrestrial genetic resources and the Seed Treaty, which apply only on a subset of species relevant to agriculture and food security. Both are the main elements of the access and benefit sharing framework (**Figure 1**). The main objectives of ABS framework are summed up in the Article 2 of the CBD: to insure "conservation of biological diversity, the sustainable use of its components and the equitable sharing of benefits arising from the utilization of genetic resources" (CBD, 1992). The Seed Treaty has been designed as a sector-specific reply to the CBD (Esquinas-Alcazar et al., 2013; Manzella, 2013) taking into consideration the need of a global commons to counteract loss of agricultural biodiversity and insure food security. It was also perceived as a global effort to counteract the trend in privatization of PGRFA, including the challenge associated with recognition of the State sovereignty over genetic resources highlighted by the CBD (Halewood et al, 2013). The Seed Treaty remains one of the most remarkable attempts to create a global commons around phytogenetic resources that recognize farmers as essential for their conservation and sustainable use (FAO, 2010; Halewood, 2013). It also aims at facilitating access to plant genetic resources for farmers, conservationists, breeders, scientists, and teachers. It is a result of a multi-decade process of international negotiations

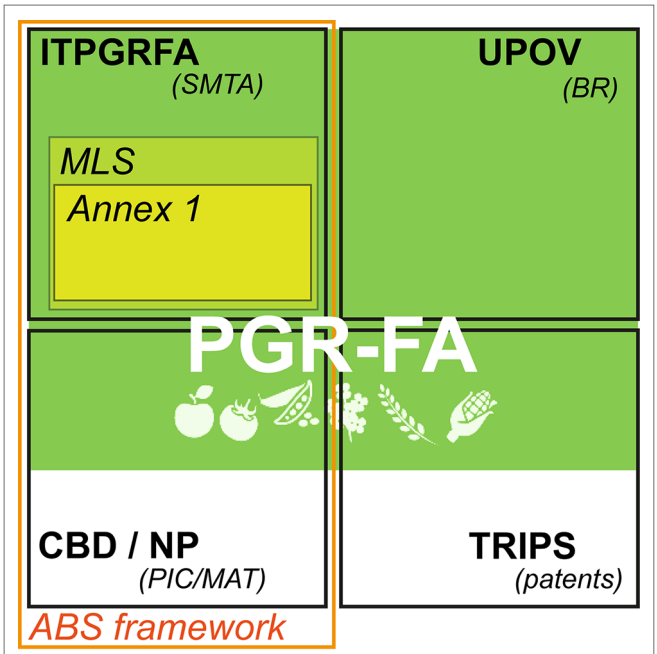

FIGURE 1 | The regime complex regulating Plant Genetic Resources for Agriculture (PGRFA). ITPGRFA, International Treaty for Genetic Resources for Food and Agriculture; SMTA, Standard Material Agreement; MLS, Multi-lateral System; UPOV, International Union for the Protection of New Varieties of Plants; BR, Breeder's right; CBD, Convention for Biodiversity; NP Nagoya Protocol; PIC/MAT, Prior Informed Consent/Mutually Agreed Terms; TRIPS, Agreement on Trade-Related Aspects of Intellectual Property Rights; ABS Access and Benefit Sharing.

that constrained its design (Halewood et al., 2013). For example, the boundaries of the common are strictly limited. The core of the Seed Treaty's common, the multilateral system, comprises a pool covering 64 of some of the most important species for agriculture. These 64 species, listed in the annex 1 of the treaty, contribute to an estimated 90% of calories, fat, protein, and weight consumed worldwide (ITPGRFA, 2004; Khoury et al., 2014). The multilateral system is often referred to as an example of global management system of the global common pool of resources (Halewood et al., 2013). Noteworthy, as a result of difficult and protracted negotiations, it only represents a fraction of the entire PGRFA (Manzella, 2013; Khoury et al., 2014). In fact, species listed in annex 1 are only part for the multilateral system when exclusively used for food or feed purposes and when those resources are under the "national governments management and control systems" (ITPGRFA, 2004). Some voluntary inclusions to the multilateral system are also possible. In addition, the multilateral system also excludes material that is declared "under development." Some important key agricultural species are not in the annex 1 (like coffee, soybean, or sugarcane), leading to some future discussion about extension or suppression of the annex 1.

Any PGRFA falling out of the scope of the Seed Treaty and not ruled by any other intellectual property regime would then eventually be regulated by the CBD and its Nagoya Protocol. Under the Nagoya protocol, the sovereignty of the country of origin is prevalent, and each single resource exchange negotiated on a case-by-case basis. All species within the multilateral system are governed by a standard material transfer agreement (SMTA) whereas the Nagoya Protocol regulates access to the resources based on a system of bilateral agreements between countries, using prior informed consent and mutually agreed terms (PIC/MAT). The SMTA used in the Seed Treaty is a standardized contract that allows a facilitated exchange of resources between signatories. Also, being the result of complex negotiations (Esquinas-Alcazar, 2013), it allows coordination between the global/international level and local stakeholders. One of its specificity is to set a default rate of benefits to be given to a third party, namely, a fiduciary fund managed by the FAO.

In a similar way to the CBD, the Seed Treaty by definition focuses on physical genetic resources: "any material of plant origin, including reproductive and vegetative propagating material, containing functional units of heredity" (ITPGRFA, 2004). However, it remains unclear to which extent the benefit sharing obligations included in the SMTA of the multilateral system do also concern obligations toward digitally derived data (often referred to as "digital sequence Information," DSI) (CBD/COP/DEC/XIII/16, 2016). Considering genetic resources exclusively as a material entity (mostly germplasm, seeds, seedlings…) may misjudge the modern practices related to GRFA and the exact nature of what is being "extracted" from these. This potentially precludes these instruments to adapt to today's modalities of use of the genetic resources: entities that are primarily mined to generate large amounts of (digital) data resulting from the use of various "omics" approaches. Previous to the digitization of genetic resources, the material-centric definition of PGRFA has already been criticized by some scholars proposing an alternative governance framework of PGRFA, which would have valued natural information (Vogel, 2011; Ruiz Muller, 2015).

A complex set of partially overlapping international legally binding instruments frame intellectual properties of PGRFA that have distinct underlying principles and aims (**Figure 1**, Roa-Rodríguez and van Dooren, 2008). The main relevant instruments for PGRFA are trade secret protection, patents, breeder's rights, copyright, and sovereign right over generic resources (for a comprehensive review, see Winter, 2013). Either one or both physical (seeds) and informational (genomic sequences) entities could in principle be privatized under those regimes (Winter, 2013; Roa et al., 2016). As a consequence, a single PGRFA could in theory be privatized based on a whole range of criteria/justifications (inventivity, genetic "potential," country of origin…) depending whether their informational or physical (or both) aspects are being considered and which regime is considered. There is a large body of work commenting on advantages and limits of each of these instruments, especially on the extent to which the global trend to privatize genetic resources impact on the PGRFA common (Dedeurwaerdere, 2013; Winter, 2013). It appears therefore that negating the hybrid status of PGRFA: both a physical and informational commodity makes it hard to design a policy framework that could fit in this "regime complex" (Raustiala and Victor, 2004) in order to guarantee access and sharing of the potential benefits. At first, an appropriate PGRFA definition seems therefore necessary to adapt to the actual state of scientific progress.

Since 2016, debates about the status of DSI has gained prominence in several international circles, including the ABS framework: the Seed Treaty (ITPGRFA, 2015; Manzella, 2016), the CBD, but also the Convention on International Trade of Endangered Species, the Pandemic Influenza Preparedness Framework of the World Health Organization, and the United Nations Convention on the Law of the Sea. This triggered a great deal of confusion and a subsequent surge of analyses and reports (CBD/COP/DEC/XIII/16, 2016; Marden, 2017; Welch et al., 2017; Heinemann et al., 2018; Laird and Wynberg, 2018). The development of synthetic biology, in other words, our increasing abilities to read and write DNA (Chari and Church, 2017), has cast fear on the possibilities to overrun physical access. However, it is possible that the DSI issue only brought to light a pre-existing ontological weakness (or unresolved long-standing tension) of the genetic resources definition in international agreements (Deplazes-Zemp et al., 2018; Marden, 2018; Prathapan et al., 2018). Here, I try to explain why a merely technical evolution that allowed a more exhaustive description of the PGRFA, namely, high-throughput sequencing of genetic information (and other "omics" data), has led to challenge the very basic fundaments of PGRFA governance and describe some possible ways forward.

DIGITAL SEQUENCE INFORMATION: ANOTHER FACE OF "BIG DATA"

Until recently, the terminology "DSI" was mostly unknown to a majority of scientists (Heinemann et al., 2018). In addition, it still remains largely unclear whether DSI should be only restricted to nucleotide sequences ("genomic information") or should also integrate other omics data like other nucleic acids, methylation status, metabolites, or even phenotypic data (Halewood et al., 2018a). Independently of the unavailability of any internationally agreed definition, genomics alone generates petabases (10^{15}) of data (i.e., nucleotide sequences) every year (www.ncbi.nlm.nih.gov/sra) and is predicted to soon exceed other "big data" science in size and complexity (Stephens et al., 2015; Heinemann et al., 2018). The quick rate of DSI generation emphasizes the potential need for a global standardized infrastructure to ensure long-term data preservation (Leonelli et al., 2013). Independently of the speed of knowledge and data generation, the "digitality" of genomic data seems trivial in practice, and DSI could well be considered as presenting most of the attributes of other "digital artifact" produced in other domains, where alternative governance models have already been implemented successfully (Kallinikos et al., 2013). Research on PGRFA also leads many initiatives to open possibilities of DSI management globally, like DivSeek for crop genomics data (www.divseek.org) or GODAN for phenotypic data (www.godan.info). Similarly, conservation of PGRFA tends to include increasing amounts of DSI, like in the DNA barcoding of life initiative (http://www.boldsystems.org/), "local" initiatives like the sequencing of genomes of an entire botanical garden (Liu et al., 2019), or major efforts from the Consortium of International Agricultural Research Centers (CGIAR) to "digitally curate" their collections (Halewood et al., 2018b). Ambitious projects of large-scale genome sequencing, like the "Earth BioGenome project" planning to sequence not less than 10 million eukaryotic species, will also bring new insights likely to be relevant for food and agriculture (Lewin et al., 2018).

The prominence of big "omics" data in biological science has not only challenged the way science is done and shared but also its underpinning philosophy (Leonelli, 2014). At odds with the increasing complexity of the instruments ruling on intellectual property over the last 30 years, biology has gradually favored opening access to the public research data and results (Strasser, 2011; Sullivan, 2004). This has recently crystallized in various policy guidelines worldwide (Wilkinson et al., 2016) that are also widely advocated in synthetic biology [OpenPlant (BioBricks Foundation), 2015]. In this context, promoting open data is essential, but the "digital divide" inherent to modern use of information and communication technologies still must be considered (Bastow and Leonelli, 2010; Bezuidenhout et al., 2017). Inequalities in data access, infrastructures and experts should not stretch the already relatively libertarian design of the Seed Treaty (Thomas, 2014). Bezuidenhout and colleagues suggest that inequalities amongst various stakeholders (farmers, breeders, researchers, consumers) should be better integrated when it comes to build an effectively open data framework, in a very similar way to Sen's approach to capability of human wellbeing (Sen, 1999). Open science (and open data) has been critically considered as shared between various owners that have a common monopoly on investments and on use of the openly accessible knowledge (Callon, 1994; Stengel et al., 2009). In other words, "open science" does not necessarily mean "fair science," and "access to" can differ greatly from "utility of" DSI (Bezuidenhout et al., 2017).

A similar debate exists in synthetic biology about digital-only information originating from genomics datasets. Alternative IP models emerged to regulate exchange of DNA "parts" [OpenPlant (BioBricks Foundation), 2015; Welch et al., 2017]. There, a

two-tier model distinguishing non-commercial technology from high-potential output was designed to maximize sharing of biomaterials and associated data. This approach was designed to answer the needs of this very specific research community (SynBio), and more work is needed to show to which extent that it might be transferable to PGRFA and breeding context at large.

The ambitious goal of the Seed Treaty is to allow "conservation and sustainable use of PGRFA, the fair and equitable sharing of the benefits arising from their use (…) for sustainable agriculture and food security" (Art. 1, ITPGRFA, 2004). These goals can be achieved, however, only with a more comprehensive and a better understanding of the way digitization has changed practices. When designing PGRFA governance, care should be taken to provide not only clear modalities of access and exchange of data, but also to the capabilities of each stakeholder involved. This would in turn allow an actual share of benefits (being monetary or not) from the global biodiversity for food and agriculture.

SPECIFICITIES OF DSI-PGRFA USE IN PLANT BREEDING

Plant research and crop improvement are largely dependent on access to DSI, being genotypic or phenotypic data (Spindel and McCouch, 2016; Halewood et al., 2018a). The Seed Treaty recognizes that exchange of information is a "non-monetary" benefit. However, given that the treaty's design largely preceded most of the genomics' developments, it remains unclear, to which extent this information exchange is considered in daily practice (Welch et al., 2017; Marden, 2018). Interestingly, some unique facets of the PGRFA are often overlooked when it comes to using DSI for modern breeding. PGRFA is a multifaced concept, involving many actors and being attached to a vast diversity of socio-economical values, and could be considered as a unique type of cultural commons (Ostrom and Hess, 2007; Madison et al., 2010; Halewood, 2013). Indeed, usage of PGRFA in a breeding program does not usually exhaust the resource (non-rivalry), but rather improves its intrinsic value and can even renew interest for its conservation. In addition, DSI originating from PGRFA will be open to all (non-exclusionary), even though this largely depends on who is able to perform the actual sequencing/phenotyping or which intellectual property regime may apply (Winter, 2013). Therefore, DSI originating from PGRFA need a tailored "new commons" concept to be adjusted to their particular hybrid status, and an extension of the ITPGRFA-framework seems the most pragmatic way to allow such a change of paradigm. DSI from PGRFA differs from the classic views on natural resources or cultural commodities by at least two main aspects:

- An optimal breeding value will be achieved, for example, during genomic selection, by merging pre-breeding data of multiple accessions. There is a necessary mixing and computing of large amounts of diverse accessions and lines in order to provide the targeted genetic progress or improved breeding values (Spindel and McCouch, 2016). This, in turn, will make the exact contribution of every single used "accession" hardly tractable. Indeed, one of the triggers of the onset of the multilateral system was the widely recognized spread of most of the plants used for food and feed worldwide (ITPGRFA, 2004). DSI add one degree of complexity to this pre-existing issue.
- The raise of synthetic biology, or more precisely the foreseen capacities of *de novo* synthesizing very large DNA fragments, even though not extensively used in breeding so far (Heinemann et al., 2018; Aubry and Eigenmann, 2019) disrupted the link between the material (germplasm) and its derived products. Despite being a very efficient system for describing and protecting DNA sequences for patents, it remains unclear how diverse and how pervasive any given intellectual property system should apply to DSI from PGRFA. For example, how easily could a codon-optimized resistance gene originating from a cryptogamic mushroom that is transformed into a modern variety of wheat be traced back to the organism it was first identified? Could intellectual property systems protect complex multi-gene networks that are essential for crop stress or pathogen resistance (Hickman et al., 2017)? How relevant is the protection or retention of data from crop pathogens that are constantly evolving and often represent global threats on agriculture (Sánchez-Vallet et al., 2018)?

The existing policy framework accommodates badly with the non-static, widely spread, non-rivalrous, and often non-exclusionary characters of DSI from PGRFA. There are fundamental differences between resources (to be extracted), natural genetic resources (to be extracted and valued), and PGRFA (to be primarily mixed/crossed to increase variability and selected in the process of breeding). These specificities need to be acknowledged when trying to improve coherence over the global governance of DSI-PGRFA.

Characterization/sequencing of PGRFA is regularly performed on cultivars, landraces, farmer's breeds, or even crop wild relatives. This aims at linking phenotype and genotype and generally produces large amounts of (digital) data. Ultimately, the goal is to enable prediction of phenotypes based on genome-wide variability. This technique is referred to as "genomic selection" (Hamblin et al., 2011; Spindel and McCouch, 2016). Pan-genomes, genomes, transcriptomes, metabolomics, and phenotypic data can be used in genome-wide association studies (GWAS) to identify relevant traits, being a single allelic variant that is linked to an agronomic trait or to gene networks (Lipka et al., 2015; Halewood et al., 2018b). Genotyping-by-sequencing and GWAS frameworks were applied based on genome variability in a diverse array of crops like maize (Yano et al., 2016), sorghum (Morris et al., 2013), pearl millet (Varshney et al., 2017), chickpea (Basu et al., 2018), peanut (Zhang et al., 2017), banana (Sardos et al., 2016), cassava (Kayondo et al., 2018; Zhang et al., 2018), and cowpea (Burridge et al., 2017). Metabolite-based GWAS was also reported as an important tool to improve genomics-assisted selection for crop improvement (Fernie and Schauer, 2009; Luo, 2015). Increasing amounts of research programs are mining the genetic diversity already collected and readily available from gene banks. Successful attempts allowed to identify the genetic basis of traits responsible for fragrance in rice (Daygon et al., 2017), underlying genetics responsible for pearl millet drought resistance (Varshney

et al., 2017), or loci encoding morphological diversity in barley (Milner et al., 2018). All of these genomic techniques allowed a better description (high-resolution fingerprinting) of the overall genetic diversity existing in each germplasm that, in turn, improve identification of relevant traits and allow a better breeding prediction and efficiency (Varshney et al., 2012). This ultimately helps ensuring a sustainable use of the PGRFA to provide crops that are locally adapted, resilient to various biotic and abiotic stresses, and necessary to maintain high levels of food security.

Noteworthy, identification and characterization of novel traits have been possible by merging several hundreds of accessions globally. The modalities of genomic data (DSI) use make traceability irrelevant: the value lies in the amounts of data analyzed, rarely in a single accession. However, exploiting the existing diversity collected in gene banks does not necessarily acknowledge the previous work of breeders and farmers during the course of agricultural history, and taking into consideration these resources as mere data-providing artifacts ("bulk of genes") may also exclude central socio-economical relationship of farmers to their crops (Thomas, 2014; Bonneuil, 2019). Continuous exchange of genetic material has shaped a large majority of the breeding programs and follows self-established decentralized rules specific to every crop. However, it is unclear how the raise and diffusion of genomic data may integrate with these already existing structures, as well as their influence on the relationship between large and small breeders, and finally how an increasing amount of freely available data might influence practices. Several initiatives, like DivSeek (McCouch et al., 2013), have tried to provide a global accessible infrastructure to catalogue the world's seed and derived genomic data collections.

ASSESSMENT OF POLICY OPTIONS: GOVERNING THE FUTURE OF PGRFA

I have shown here actual modalities and challenges in considering some aspects of PGRFA as big data and try to evaluate the impact of digitization of PGRFA on the existing international policy framework. The various models described below extend on ongoing negotiations and by far are not meant to be exhaustive. I will evaluate *ex ante* their practicality and potential consequences (**Table 1**).

Ignoring DSI: *De Facto* Open Access for Any Digital Information

Technically, the easiest solution is to ignore the DSI issue and to defend a *status quo*: keep the billions of sequenced DNA information away from the scope of any internationally binding treaty. A more holistic approach has been proposed, using the prominent situation of the CGIAR, to try inspiring new standards and soft norms to the field—for example, extension of the Global Information System (GLIS) infrastructure (Ker et al., 2013), or association of open-access passport data or digital object identifier (DOI) systematically to each shared element from a PGRFA (Manzella, 2016; Roa et al., 2016; Halewood et al., 2018a). For accessions not contained in the multilateral system, it has also been suggested to exclude non-commercial research from any data-access restriction (Biber-Klemm et al., 2010). Indeed, there are obvious contradictions when limiting access to data in conservation biology: this could possibly impair our understanding of the extent of biodiversity loss (also observed for cultivated plants and their relatives) and, therefore, limits our

TABLE 1 | Overview of possible options to include DSI-GRFA into existing genetic resources regulatory regime and their possible advantages and limits.

DSI governance models		Advantages	Limits	Challenges
Exclusion		Easy implementation	Do not reflect the actual state-of-the-art of the use of GRFA Risk of obsolescence of the treaties on GR globally	Will or have been already criticized by providers and mega-diverse countries as having possible large consequences on the ITPGRFA and CBD
Extension of the SMTA to DSI		Might make possible a better traceability and guarantee BS on DSI originating from specific GRFA	Practically almost impossible to set up Practicability will limit or impair overall use of GR(FA) and the rate of crop improvement.	Very hard to be globally implemented even though protection of DNA sequences well established for patent
Extending the common	*Subscription model*	Relatively easy within ITPGRFA. Might even be an incentive to extend the multilateral system	Limit already existing with the ITPGRFA. For example, limitation to the annex 1 crops and low or no participation to the Fund	Extend the scope of the treaties to any DSI involved in agriculture Reaching an international consensus
	Bounded openness	Simplify the access to GR(FA) Transparency on the benefits	Might hurt principles of sovereignty Large discretionary power of patent offices	Totally ignore potential socio-economical values of PGRFA and their associated DSI
	Knowledge common	Relative ease of use once running Allow an easy assessment of the global fairness of the system	Might be difficult to convince all stakeholder to take part	Would require a global effort to normalize multilateral governance on GRFA
Common heritage of humankind		Inherently open access	Have been shown in other fields not to be protecting fairness and taking into consideration capabilities of all stakeholders	Largely idealistic given the history of "common heritage" policy

This table provides a large panorama of the possible policies, from the easiest (exclusion of DSI) to the broadest (DSI as common heritage) models.

option to counteract it (Deplazes-Zemp et al., 2018; Prathapan et al., 2018; FAO, 2019).

As described in the previous section, sustainable use and conservation of PGRFA will require maximizing the amount of data available. For example, the necessary conservation of crop wild relatives (CWR) and their description are essential for expanding the gene pools used in modern crop breeding (Brozynska et al., 2016; Gruber, 2016; Capistrano-Gossmann et al., 2017; Dempewolf et al., 2017).

Ignoring the digitality of PGRFA might be the most pragmatic way of processing, in view of the quantity of already freely available data in public databases, but it also vastly ignores issues related to inequalities of access and capacities to value these data for a sustainable use in agriculture. Therefore, it remains to be evaluated what would be the exact consequences—for example, on global food security, of a purely libertarian stand on DSI-PGRFA. Similarly, consequences of any regulation, or uncertainty about potential forthcoming regulations, on innovation are hardly predictable. Given the actual stand of the discussion, this option is unlikely to satisfy all parties, unless maybe guaranteeing a global access to any DSI from (any) PGRFA, including data from germplasm not necessarily outside the multilateral system of the Seed Treaty crops.

Extension of the Standard Material Agreements to DSI

As shown in the previous section, the specific modalities of DSI use in breeding make any restriction to the access to DSI particularly difficult and probably irrelevant: the potential value of a PGRFA results very often from its collective use and changes with time. In addition, issues related to the actual jurisdiction in which a PGRFA could originate, and how common any given trait, variant, or metabolite is to another PGRFA, make any possible tracing system elusive. For example, meta-studies of soil microorganisms would hardly trace back to actually described species, nor would a specific microbe strain be doubtlessly associated with any given country of origin. Despite these difficulties, some attempts to track DSI, or at least to improve DSI transparency, are under discussion at the database level (Scott and Berry, 2016) and on various policy fora such as the Intergovernmental Committee on Intellectual Property and Genetic Resources and the Traditional Knowledge and Folklore of the World Intellectual Property Organization (WIPO, 2018). Beyond the obvious political difficulties in amending a new SMTA that would satisfy all parties, practically, the underlying peculiarities of the biology and the genetics associated with DSI will make any enforcement impossible and potentially counterproductive. Alternatively, if DSI from PGRFA have to be "incorporated" as benefits as in the terms of Art 13.2.d of the Seed Treaty, downstream uses of these data would have to be understood and acknowledged to try keeping the initial intension of this instrument regarding their sustainable use. Concerning species outside the scope of the multilateral system, the issue regarding DSI is probably even more pronounced, and access to the data might only be a matter of voluntary contribution of the DSI producers to the public databases.

In any case, in view of the DSI specific properties (non-rivalry, enhanced value through their use and geographic "triviality"), it might become relevant in the next future to reconsider—at least concerning DSI—whether the access and the benefit sharing should remain coupled the way they are now.

Extending the Commons

During the 6th and 7th sessions of the Governing Body of the Seed Treaty, an extension of the multilateral system to a subscription model has been discussed (ITPGRFA, 2015; ITPGRFA, 2017). Despite being part of another discussion about possible general improvement of the instrument itself, this discussion indirectly revealed the multilateral system of the Seed Treaty prone to fit with the complexity of DSI, especially compared with other ABS instruments (Halewood et al., 2018a). However, the exact modalities to possibly integrate DSI to such a system could greatly influence the way PGRFA would be further used/shared, the behaviors of various stakeholders, and finally the relevance of the existing instruments. In view of the complexity of the regulation of genetic resources, whatever the next genetic resource-related governance design would be, this will necessarily have influences on other fields. For example, it is unclear how much the rather restricted commons designed by the World Health Organization as especially dedicated to the governance of the influenza virus (and includes DSI) might serve as a model for other treaties (Fidler and Gostin, 2011). To summarize, three alternative multilateral models could be envisaged to cope with DSI (**Table 1**):

- The subscription model as a "simple" way to consider DSI. Ongoing discussion to extend the multilateral system could represent a solution to integrate the "informational" component of PGRFA into the scope of the Seed Treaty while keeping administrative burden low. A front payment would allow access to a multilateral system DSI database of PGRFA (like GLIS). Given there would be no "parallel system" running (to avoid free-riding), this model could allow more transparency and fairness. However, some parties already announced they would not participate to any subscription system if DSI were to be taken into consideration (ITPGRFA, 2017). Such adaptation of the multilateral system to the modern modalities of DSI use should be taken as a unique chance to make the treaties closer to modern practice. A subscription model might also be able to uncouple the actual DSI use and the probable commercialization of the derived information. In any case, to have a chance to be globally accepted and implemented, this will require a high level of trust from all stakeholders.
- An alternative multilateral system, the "bounded openness" has been advocated as a way to integrate DSI as natural "intangible" information (Ruiz Muller, 2015; Vogel et al., 2018). One of the basic fundamental point of this model is the new definition of genetic resources as "any information, derived from nature, but not limited to, hereditary units, metabolites, proteins, enzymes, prions, phenotypic expression and non-human cultures" (Ruiz Muller, 2015). In addition, this model proposes a shift of the disclosure of any information (including DSI) from a given resource, up to the point of its commercial use or patenting (when it happens) and following standardized

royalties rates (Ruiz Muller, 2015). The rationale of such a model is that local case-to-case deals (as in the current Nagoya Protocol framework) are probably less fair, or at least less transparent than a global governance. Arguably, this model might be practically extremely complicated and would provide a strong discretionary power to the patent offices that might not follow the same (ecological, cultural, scientific, educational…) goals as other instruments like the Seed Treaty or the CBD. Also, it is unclear to which extent such a "bounded openness" regime might interact with other intellectual property regimes like farmer's or breeder's right, or when PGRFA bulks are used collectively in gene bank genomics approaches. Another "flavor" of such model has recently been proposed for marine genetic resources in areas beyond national jurisdiction, with default open access and an optional payable embargo period on data and samples (Vanagt et al., 2019). Concerning PGRFA, some stakeholders may find such models that consider natural information too reductionist and not embracing the socio-economical relationship that could exist between PGRFA and the population or group they may originate from.

- Another possible way of dealing with the increasing complexity of PGRFA governance is to try building an extensive "knowledge commons," that can include all possible aspects of PGRFA (Winter, 2013), i.e., a global tax associated with any value-generating object or activity based on PGRFA (Halewood et al., 2018a; Halewood et al., 2018b). This again may require an adjustment of PGRFA definition to move away from the material-centric view and take into consideration the informational nature of the PGRFA. The main advantage here is the uncoupling of the access and use of the PGRFA and derived DSI. Taxing users, institutions, companies, or even countries will provide a possibly simpler system but also requires political consensus *via* new multilateral agreements.

DSI as Common Heritage of Mankind?

The preamble of the Seed Treaty recognizes the PGRFA as a "common concern of all countries" (ITPGRFA, 2004). This precise formulation responded to the early days of multilateralism, where the Moon, the outer space, and the deep ocean were largely inaccessible and legally defined as common good of mankind. Despite the maybe quixotic goals that were initially aimed at, one can wonder to which extent any genetic resource and the information they hold could for example reasonably be managed under a protection similar to the cultural or natural heritages (UNESCO Convention Concerning the Protection of the World Cultural and Natural Heritage, 1972). However, it is clear that the actual inclusive governance of the genetic resources was designed in response to the earlier failures of multilateral approaches to protect biodiversity globally (Smouts, 2005; Blasiak et al., 2018). Preserving genetic resources is still a global priority, but this should not necessarily be taken as an argument to transform PGRFA as purely monetary commodity depleted of any ethical or sociological value. Proof is still to be made to which extent PGRFA and more globally genetic resource conservation actually benefited globally from the existing governance (Prathapan et al., 2018). This holds even more true when the commodity is a string of nucleotides freely accessible online originating from the other side of the globe in a changing environment. DSI as global "open access" common good would avoid the potential complications of any attempt to track and trace DSI at a global level (including possible mechanisms that might try maintaining compliance). Considering DSI as a common good of humankind would most probably raise major opposition related to the State's sovereignties of each country on their genetic resources, as ruled in the CBD (Halewood, 2013). If considering genetic resources as a common heritage of mankind or more likely as a global public good, care should be taken to design a new inclusive form of governance that takes into consideration what exactly are these goods, how common they might be, and who exactly is the (hu)mankind.

ACTIONABLE RECOMMENDATIONS

The DSI debates in various international fora have revealed pre-existing weakness in the design of the Seed Treaty, as well as possibly in other treaties dealing with genetic resources. This has at least two main consequences: firstly, there is a need to coordinate efforts to embrace scientific progress in the genetic resource field (Laird and Wynberg, 2018). A non-reductionist and pragmatic definition of PGRFA is urgently needed. The "new" PGRFA definition would ideally become a more inclusive concept that would better acknowledge farmer's role in diversity creation and conservation (Bonneuil, 2019). Secondly, in light of what the various ongoing debates about genetic resources from many different sectors, care should be taken to understand the specificities of the PGRFA: modern breeding considers DSI-PGRFA largely in a "big data" manner, which might not be true—for example, for conservation of specific endangered species or public health. Interesting parallels can help improving the PGRFA framework, like other genetic resources originating from animals or bacteria (Dedeurwaerdere, 2013) or "classic" digital artifact governance (Stuermer et al., 2017). To allow a sustainable use of digital artifacts (DSI) originating from PGRFA (if totally uncoupled from the physical resource), some fundamental modifications of the digital infrastructure would be necessary: decentralization of the databases in modular structures and diversified funding are required to insure a resilient and fair system (Stuermer et al., 2017). Properly answering the challenges of dematerialization is a necessary condition to ensure that the ABS instruments stay relevant in the state of actual science and fulfill their objectives.

"Omics" has changed the precision and efficiency of breeding by an order of magnitude. Genomic selection and GWAS together with gene bank genomics approaches are becoming commonplace, even for some neglected and underused crops. For the Seed Treaty itself, DSI should be considered as a chance to embrace an extended multilateral approach by developing an updated and fair subscription system. However, such an approach should also carefully consider modalities of DSI generation, curation, storage, and dissemination. It will be essential to engage with various stakeholders to reduce disparities and encourage accessibility, transparency, and accountability (Bezuidenhout et al., 2017; Kaye et al., 2018). This might, in turn, reduce the "*breeding divide*" between low- or middle- and high-income countries. Large-scale deployment

of genomics facilitated by a constant decrease of technology costs, democratization of open-source analytic pipelines, and capacity building may in the long term favor a major reshuffling of the way breeding is performed in various agroecosystems. Farmer-centric participatory breeding networks promote an integrative, bottom-up vision of plant breeding (Joly and Hervieu, 2003; Bonneuil and Thomas, 2009). However local-level PGRFA productions do not accommodate well with the Seed Treaty and the multilateral system (Halewood, 2013). Supporting wider use of genomic-based technologies for on-farm and community-based breeding may possibly allow emergence of new locally adapted diversity that is essential for crop improvement (Jarvis et al., 2008; Halewood et al., 2018b). A recent large-scale study by CGIAR showed the potential of crowdsource citizen-science programs to adapt plant varieties to site-specific conditions, a challenge for smallholder farmers suffering climate change (van Etten et al., 2019).

To conclude, the management of PGRFA and more generally of genetic resources appear to be at a turning point in its history. The digitization is now an underlying parameter of negotiations over the treaty's reforms. It questions again the fragility and the limits of the Seed Treaty boundaries and capacities to trace efficiently DSI and their resources. This debate should be used as an opportunity to improve of the actual instrument in order to 1) think again what are the best possible ways to respond to the food security challenges, in other words, are any additional rule over DSI practicable? And 2) does the ABS framework, and the Seed Treaty in particular, focus on the wrong type of incentive? Alternative models of digital goods management are based on motivations to contribute to the commons pool without direct incentive from property rights. Reputation gain, learning effects or faster time to the market could be other alternative incentives to participate to the commons (Dedeurwaerdere, 2013; Stuermer et al., 2017). With the ongoing omics developments, if not correctly addressed, the "DSI issue" might threaten the stability of the Seed Treaty and the possibly the entire ABS framework. More work is needed to evaluate the relevance of the proposed models for each specific sector and the potential impact of digital "free-riding" on science, innovation, breeding, and ultimately food supply. Taking advantage of operational research methods, sustainability prediction of each particular model presented here is possible in a more quantitative way by applying robust decision-analytic tools used in other policy-making fields (Wohlfender-Bühler et al., 2016; Zheng et al., 2016). Whatever the most appropriate model of treaty-based international regulatory regime for PGRFA and their commons may be (by a reform of the existing instruments or by a new overarching treaty that would specifically fit to digital genetic resources), it appears already clearly that an increased degree of multilateralism and harmonization is necessary to align to the current practices and unravel the formidable potentials originating from digitization of PGRFA.

This review aimed at providing DSI users and providers a glimpse of the complexity of the various intertwined policies ruling PGRFA. Integration of digital information in the PGRFA policy framework will greatly depend how these DSI actors become aware of the potential impact of their daily practice on the global debate. In parallel, this may also encourage experts having access to digital infrastructures to try helping empowerment of smallholder farmer communities and local cooperative networks to "omics" techniques applied to breeding. This could be a most efficient, resilient, and decentralized model for a modern governance of PGRFA. This is essential, not only to save existing crop biodiversity, but also to create new genetic diversity that will strongly be needed to tackle some of the major global challenges humanity currently faces like climate change and food security.

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REFERENCES

Aubry, S., and Eigenmann, C. (2019). New challenges to digitization of genetic resources for food and agriculture. *AGRARForschung* 10, 122–127.

Bastow, R., and Leonelli, S. (2010). Sustainable digital infrastructure. Although databases and other online resources have become a central tool for biological research, their long-term support and maintenance is far from secure. *EMBO Rep.* 11, 730–734. doi: 10.1038/embor.2010.145

Basu, U., Srivastava, R., Bajaj, D., Thakro, V., Daware, A., Malik, N., et al. (2018). Genome-wide generation and genotyping of informative SNPs to scan molecular signatures for seed yield in chickpea. *Sci. Rep.* 8, 13240. doi: 10.1038/s41598-018-29926-1

Bezuidenhout, L. M., Leonelli, S., Kelly, A. H., and Rappert, B. (2017). Beyond the digital divide: towards a situated approach to open data. *Sci. Public Policy* 44, 464–475. doi: 10.1093/scipol/scw036

Biber-Klemm, S., Martinez, S., and Jacob, A. (2010). *Access to genetic resources and sharing of benefits - ABS Program 2003–2010.* Report of the Swiss Academy of Sciences, Bern, Switzerland.

Blasiak, R., Jouffray, J.-B., Wabnitz, C. C. C., Sundström, E., and Österblom, H. (2018). Corporate control and global governance of marine genetic resources. *Sci. Adv.* 4, eaar5237. doi: 10.1126/sciadv.aar5237

Bonneuil, C. (2019). Seeing nature as a 'universal store of genes': how biological diversity became 'genetic resources', 1890–1940. *Stud. Hist. Philos. Sci. Part C Stud. Hist. Philos. Biol. Biomed. Sci.* doi: 10.1016/j.shpsc.2018.12.002

Bonneuil, C., and Thomas, F. (2009). *Gènes, pouvoirs et profits: recherche publique et régimes de production des savoirs de Mendel aux OGM*. Versailles, France: Editions Quae.

Brozynska, M., Furtado, A., and Henry, R. J. (2016). Genomics of crop wild relatives: expanding the gene pool for crop improvement. *Plant Biotechnol. J.* 14, 1070–1085. doi: 10.1111/pbi.12454

Burridge, J. D., Schneider, H. M., Huynh, B.-L., Roberts, P. A., Bucksch, A., and Lynch, J. P. (2017). Genome-wide association mapping and agronomic impact of cowpea root architecture. *Theor. Appl. Genet.* 130, 419–431. doi: 10.1007/s00122-016-2823-y

Callon, M. (1994). Is science a public good? Fifth Mullins Lecture, Virginia Polytechnic Institute, 23 March 1993. *Sci. Technol. Hum. Values* 19, 395–424. doi: 10.1177/016224399401900401

Capistrano-Gossmann, G. G., Ries, D., Holtgräwe, D., Minoche, A., Kraft, T., Frerichmann, S. L. M., et al. (2017). Crop wild relative populations of Beta vulgaris allow direct mapping of agronomically important genes. *Nat. Commun.* 8, 15708. doi: 10.1038/ncomms15708

CBD/COP/DEC/XIII/16, 2016. Decision adopted by the conference of the parties to the convention on biological diversity. Available at: https://www.cbd.int/doc/decisions/cop-13/cop-13-dec-16-en.pdf [Accessed March 1, 2019]

CBD, 1992. Convention on biological diversity. Available at: http://www.cbd.int/.

Chari, R., and Church, G. M. (2017). Beyond editing to writing large genomes. *Nat. Rev. Genet.* 18, 749–760. doi: 10.1038/nrg.2017.59

Daygon, V. D., Calingacion, M., Forster, L. C., Voss, J. J., De, Schwartz, B. D., Ovenden, B., et al. (2017). Metabolomics and genomics combine to unravel the pathway for the presence of fragrance in rice. *Sci. Rep.* 7, 8767. doi: 10.1038/s41598-017-07693-9

Dedeurwaerdere, T. (2013). "Institutionalizing global genetic resource commons for food and agriculture," in *Crop Genetic Resources as a Global Commons* (Routledge, UK: Bioversity International), 368 –391.

Dempewolf, H., Baute, G., Anderson, J., Kilian, B., Smith, C., and Guarino, L. (2017). Past and future use of wild relatives in crop breeding. *Crop Sci.* 57, 1070. doi: 10.2135/cropsci2016.10.0885

Deplazes-Zemp, A., Abiven, S., Schaber, P., Schaepman, M., Schaepman-Strub, G., Schmid, B., et al. (2018). The Nagoya Protocol could backfire on the Global South. *Nat. Ecol. Evol.* 2, 917–919. doi: 10.1038/s41559-018-0561-z

Esquinas-Alcázar, J. (2005). Science and society: protecting crop genetic diversity for food security: political, ethical and technical challenges. *Nat. Rev. Genet.* 6, 946–953. doi: 10.1038/nrg1729

Esquinas-Alcazar, J., Hilmi, A., and Lopez-Noriega, I. (2013). "A brief history of the negotiation on the treaty on plant genetic resources for food and agriculture," in *Crop Genetic Resources as a Global Commons*, vol. 15. (Routledge, UK: Bioversity International) , 135–148.

FAO, 2010. Second report on the world's plant genetic resources for food and agriculture. Available at: http://www.fao.org/3/i1500e/i1500e00.htm

FAO, 2019. The state of biodiversity for food and agriculture. Available at: http://www.fao.org/state-of-biodiversity-for-food-agriculture/en/.

Fernie, A. R., and Schauer, N. (2009). Metabolomics-assisted breeding: a viable option for crop improvement? *Trends Genet.* 25, 39–48. doi: 10.1016/j.tig.2008.10.010

Fidler, D. P., and Gostin, L. O. (2011). The WHO pandemic influenza preparedness framework. *JAMA* 306 (2), 200–201. doi: 10.1001/jama.2011.960

Gruber, K. (2016). Re-igniting the green revolution with wild crops. *Nat. plants* 2, 16048. doi: 10.1038/nplants.2016.48

Halewood, M. (2013). What kind of goods are plant genetic resources for food and agriculture? Towards the identification and development of a new global commons. *Int. J. Commons* 7, 278. doi: 10.18352/ijc.412

Halewood, M., Chiurugwi, T., Sackville Hamilton, R., Kurtz, B., Marden, E., Welch, E., et al. (2018a). Plant genetic resources for food and agriculture: opportunities and challenges emerging from the science and information technology revolution. *New Phytol.* 217, 1407–1419. doi: 10.1111/nph.14993

Halewood, M., Lopez-Noriega, I., and Louafi, S. (2013). "The global crop commons and access and benefit-sharing laws," in *Crop Genetic Resources as a Global Commons* (Routledge, UK: Bioversity International), 1–36.

Halewood, M., Lopez Noriega, I., Ellis, D., Roa, C., Rouard, M., and Sackville Hamilton, R. (2018b). Using genomic sequence information to increase conservation and sustainable use of crop diversity and benefit-sharing. *Biopreserv. Biobank.* 16, 368–376. doi: 10.1089/bio.2018.0043

Hamblin, M. T., Buckler, E. S., and Jannink, J.-L. (2011). Population genetics of genomics-based crop improvement methods. *Trends Genet.* 27, 98–106. doi: 10.1016/j.tig.2010.12.003

Harlan, J. R. (1975). Our vanishing genetic resources. *Science* 188, 617–621. doi: 10.1126/science.188.4188.617

Heinemann, J., Coray, D., and Thaler, D. (2018). Fact-finding and scoping study on "digital sequence information" on genetic resources for food and agriculture. Available at: https://www.cbd.int/doc/notifications/2017/ntf-2017-115-abs-en.pdf [Accessed March 1, 2019].

Hickman, R., Van Verk, M. C., Van Dijken, A. J. H., Mendes, M. P., Vroegop-Vos, I. A., Caarls, L., et al. (2017). Architecture and dynamics of the jasmonic acid gene regulatory network. *Plant Cell* 29, 2086–2105. doi: 10.1105/tpc.16.00958

ITPGRFA, 2004. International treaty on plant genetic resources for food. FAO. Available at: www.fao.org/3/a-i0510e.pdf%0A%0A.

ITPGRFA, 2015. Sixth session of the governing body of the ITPGRFA. Available at: http://www.fao.org/3/a-mo938e.pdf

ITPGRFA, 2017. Seventh session of the governing body of the ITPGRFA. Available at: http://www.fao.org/3/MV606/mv606.pdf.

Jarvis, D. I., Brown, A. H. D., Cuong, P. H., Collado-Panduro, L., Latourneerie-Moreno, L., Gyawali, S., et al. (2008). A global perspective of the richness and evenness of traditional crop-variety diversity maintained by farming communities. *Proc. Natl. Acad. Sci.* 105, 5326–5331. doi: 10.1073/pnas.0800607105

Joly, P., and Hervieu, B. (2003). Merchandising of living. For pooling research in genomics. *Futuribles* 292, 5–29.

Kallinikos, J., Aaltonen, A., and Marton, A. (2013). The ambivalent ontology of digital artifacts. *MIS Q.* 37, 357–370. doi: 10.25300/MISQ/2013/37.2.02

Kaye, J., Terry, S. F., Juengst, E., Coy, S., Harris, J. R., Chalmers, D., et al. (2018). Including all voices in international data-sharing governance. *Hum. Genomics* 12, 13. doi: 10.1186/s40246-018-0143-9

Kayondo, S. I., Pino Del Carpio, D., Lozano, R., Ozimati, A., Wolfe, M., Baguma, Y., et al. (2018). Genome-wide association mapping and genomic prediction for CBSD resistance in Manihot esculenta. *Sci. Rep.* 8, 1549. doi: 10.1038/s41598-018-19696-1

Ker, C., Louafi, S., and Sanou, M. (2013). "Building a global information system in support of the international treaty on plant genetic resources for food and agriculture," in *Crop Genetic Resources as a Global Commons*, vol. 26. (Routledge, UK: Bioversity International) , 283–309.

Khoury, C. K., Bjorkman, A. D., Dempewolf, H., Ramirez-Villegas, J., Guarino, L., Jarvis, A., et al. (2014). Increasing homogeneity in global food supplies and the implications for food security. *Proc. Natl. Acad. Sci. U. S. A.* 111, 4001–4006. doi: 10.1073/pnas.1313490111

Laird, S., and Wynberg, R. (2018). A fact finding and scoping study on digital sequence information on genetic resources in the context of the convention on biological diversity and Nagoya Protocol. Available at: https://www.researchgate.net/publication/321005788_A_Fact_Finding_and_Scoping_Study_on_Digital_Sequence_Information_on_Genetic_Resources_in_the_Context_of_the_Convention_on_Biological_Diversity_and_Nagoya_Protocol.

Leonelli, S. (2014). Data Interpretation in the digital age. *Perspect. Sci.* 22, 397–417. doi: 10.1162/POSC_a_00140

Leonelli, S., Smirnoff, N., Moore, J., Cook, C., and Bastow, R. (2013). Making open data work for plant scientists. *J. Exp. Bot.* 64, 4109–4117. doi: 10.1093/jxb/ert273

Lewin, H. A., Robinson, G. E., Kress, W. J., Baker, W. J., Coddington, J., Crandall, K. A., et al. (2018). Earth BioGenome Project: sequencing life for the future of life. *Proc. Natl. Acad. Sci. U. S. A.* 115, 4325–4333. doi: 10.1073/pnas.1720115115

Lipka, A. E., Kandianis, C. B., Hudson, M. E., Yu, J., Drnevich, J., Bradbury, P. J., et al. (2015). From association to prediction: statistical methods for the dissection and selection of complex traits in plants. *Curr. Opin. Plant Biol.* 24, 110–118. doi: 10.1016/j.pbi.2015.02.010

Liu, H., Wei, J., Yang, T., Mu, W., Song, B., Yang, T., et al. (2019). Molecular digitization of a botanical garden: high-depth whole genome sequencing of 689 vascular plant species from the Ruili Botanical Garden. *Gigascience,* 8 (4). doi: 10.1093/gigascience/giz007

Luo, J. (2015). Metabolite-based genome-wide association studies in plants. *Curr. Opin. Plant Biol.* 24, 31–38. doi: 10.1016/j.pbi.2015.01.006

Madison, M., Frischmann, B., and Stranburg, K. (2010). Constructing commons in the cultural environment. *Cornell Law Rev.* 95, 657–710.

Manzella, D. (2013). "The design and mechanics of the multilateral system of access and benefit sharing," in *Crop Genetic Resources as a Global Commons* (Routledge, UK: Bioversity International), 150–163.

Manzella, D. (2016). The global information system and genomic information: transparency of rights and obligations. Available at: www.fao.org/3/a-bq620e.pdf.

Marden, E. (2017). U.S. ratification of Plant Treaty: benefit sharing ambiguity for plant genomics researchers does not change. *Genet. Resour. Crop Evol.* 64, 1133–1139. doi: 10.1007/s10722-017-0528-y

Marden, E. (2018). International agreements may impact genomic technologies. *Nat. plants* 4, 2–4. doi: 10.1038/s41477-017-0087-4

McCouch, S., Baute, G. J., Bradeen, J., Bramel, P., Bretting, P. K., Buckler, E., et al. (2013). Agriculture: feeding the future. *Nature* 499, 23–24. doi: 10.1038/499023a

Milner, S. G., Jost, M., Taketa, S., Mazón, E. R., Himmelbach, A., Oppermann, M., et al. (2018). Genebank genomics highlights the diversity of a global barley collection. *Nat. Genet*. 51, 619–326. doi: 10.1038/s41588-018-0266-x

Morris, G. P., Ramu, P., Deshpande, S. P., Hash, C. T., Shah, T., Upadhyaya, H. D., et al. (2013). Population genomic and genome-wide association studies of agroclimatic traits in sorghum. *Proc. Natl. Acad. Sci.* 110, 453–458. doi: 10.1073/pnas.1215985110

OpenPlant (BioBricks Foundation) (2015). Towards an open material transfer agreement. Available at: https://www.openplant.org/openmta.

Ostrom, E., and Hess, C. (2007). Private and common property rights. *Indiana University, Bloomington: School of Public & Environmental Affairs Research, Paper No. 2008-11-01*. Available at SSRN: https://ssrn.com/abstract=1936062.

Prathapan, K. D., Pethiyagoda, R., Bawa, K. S., Raven, P. H., Rajan, P. D., and 172 co-signatories from 35 countries (2018). When the cure kills-CBD limits biodiversity research. *Science* 360, 1405–1406. doi: 10.1126/science.aat9844

Raustiala, K., and Victor, D. G. (2004). The Regime Complex for Plant Genetic Resources. *Int. Organ.* 58 (2), 277–309. doi: 10.1017/S0020818304582036

Roa-Rodríguez, C., and van Dooren, T. (2008). Shifting common spaces of plant genetic resources in the international regulation of property. *J. World Intellect. Prop.* 11, 176–202. doi: 10.1111/j.1747-1796.2008.00342.x

Roa, C., Hamilton, R. S., Wenzl, P., and Powell, W. (2016). Plant genetic resources: needs, rights, and opportunities. *Trends Plant Sci.* 21, 633–636. doi: 10.1016/j.tplants.2016.06.002

Rousseau, J. (1755). *Discourse on inequality*. London, UK: Penguin Classics.

Ruiz Muller, M. (2015). *Genetic resources as natural information*. Routledge London, UK. doi: 10.4324/9781315754451

Sánchez-Vallet, A., Fouché, S., Fudal, I., Hartmann, F. E., Soyer, J. L., Tellier, A., et al. (2018). The genome biology of effector gene evolution in filamentous plant pathogens. *Annu. Rev. Phytopathol.* 56, 21–40. doi: 10.1146/annurev-phyto-080516-035303

Sardos, J., Rouard, M., Hueber, Y., Cenci, A., Hyma, K. E., van den Houwe, I., et al. (2016). A genome-wide association study on the seedless phenotype in banana (Musa spp.) reveals the potential of a selected panel to detect candidate genes in a vegetatively propagated crop. *PLoS One* 11, e0154448. doi: 10.1371/journal.pone.0154448

Scott, D. and Berry, D. (2016). Genetic Resources in the age of the Nagoya Protocol and gene/genome synthesis. Report of the University of Edinburgh. Available at: https://www.cbd.int/abs/DSI-views/EdinburghUni-DSI.pdf.

Sen, A. (1999). *Commodities and capabilities*. Oxford, UK: Oxford University Press.

Smouts, M. (2005). "Du patrimoine commun de l'humanité aux biens publics globaux," in *Patrimoines naturels au Sud : territoires, identités et stratégies locales*, (Marseille, France: IRD Editions), 53–70. doi: 10.4000/books.irdeditions.4056

Spindel, J. E., and McCouch, S. R. (2016). When more is better: how data sharing would accelerate genomic selection of crop plants. *New Phytol.* 212, 814–826. doi: 10.1111/nph.14174

Stengel, K., Taylor, J., Waterton, C., and Wynne, B. (2009). Plant Sciences and the public good. *Sci. Technol. Hum. Values* 34, 289–312. doi: 10.1177/0162243907312955

Stephens, Z. D., Lee, S. Y., Faghri, F., Campbell, R. H., Zhai, C., Efron, M. J., et al. (2015). Big data: astronomical or genomical? *PLoS Biol.* 13, e1002195. doi: 10.1371/journal.pbio.1002195

Strasser, B. J. (2011). The experimenter's museum: GenBank, natural history, and the moral economies of biomedicine. *Isis.* 102, 60–96. doi: 10.1086/658657

Stuermer, M., Abu-Tayeh, G., and Myrach, T. (2017). Digital sustainability: basic conditions for sustainable digital artifacts and their ecosystems. *Sustain. Sci.* 12, 247–262. doi: 10.1007/s11625-016-0412-2

Sullivan, S. N. (2004). Plant genetic resources and the law: past, present, and future. *Plant Physiol.* 135, 10–15. doi: 10.1104/pp.104.042572

Thomas, F. (2014). Les éthiques du partage des avantages dans la gouvernance internationale de la biodiversité sauvage et cultivée. *Éthique publique* 16 (1), 1–5. doi: 10.4000/ethiquepublique.1392

UNESCO Convention Concerning the Protection of the World Cultural and Natural Heritage (1972). Available at: https://whc.unesco.org/en/convention/.

van Etten, J., de Sousa, K., Aguilar, A., Barrios, M., Coto, A., Dell'Acqua, M., et al. (2019). Crop variety management for climate adaptation supported by citizen science. *Proc. Natl. Acad. Sci. U. S. A.* 116 (10), 4194–4199. doi: 10.1073/pnas.1813720116

Vanagt, T., Broggiato, A., Lallier, L. E., Jaspars, M., Burton, G., and Muyldermans, D. (2019). "Towards an implementing agreement for marine genetic resources in international waters," in *Conserving Biodiversity in Areas beyond National Jurisdiction* (Leiden, The Netherlands: Brill), 267–297. doi: 10.1163/9789004391703_012

Varshney, R. K., Ribaut, J.-M., Buckler, E. S., Tuberosa, R., Rafalski, J. A., and Langridge, P. (2012). Can genomics boost productivity of orphan crops? *Nat. Biotechnol.* 30, 1172–1176. doi: 10.1038/nbt.2440

Varshney, R. K., Shi, C., Thudi, M., Mariac, C., Wallace, J., Qi, P., et al. (2017). Pearl millet genome sequence provides a resource to improve agronomic traits in arid environments. *Nat. Biotechnol.* 35, 969–976. doi: 10.1038/nbt.3943

Vogel, J. (2011). The economics of information, studiously ignored in the Nagoya Protocol on access to genetic resources and benefit sharing. *Law Environ. Dev. J.* 7, 52.

Vogel, J., Angerer, K., Ruiz Muller, M., and Oduardo-Sierra, O. (2018). "Bounded openness as the global multilateral benefit-sharing mechanism for the Nagoya Protocol," in *Routledge Handbook on Biodiversity and the Law*. Eds. C. McManis and B. Ong (Routledge) , London, UK, 377–394. Available at: www.lead-journal.org/content/11052.pdf.

Welch, E., Bagley, M. A., Kuiken, T., and Louafi, S. (2017). Potential implications of new synthetic biology and genomic research trajectories on the International Treaty for Plant Genetic Resources for Food and Agriculture. *Emory Legal Studies Research Paper.* Available at: https://ssrn.com/abstract=3173781.

Wilkinson, M. D., Dumontier, M., Aalbersberg, I. J., Appleton, G., Axton, M., Baak, A., et al. (2016). The FAIR Guiding Principles for scientific data management and stewardship. *Sci. Data* 3, 160018. doi: 10.1038/sdata.2016.18

Winter, G. (2013). "Knowledge commons, intellectual property and the ABS regime," in *Common Pools of Genetic Resources*, Routledge, London, UK, 285–301.

WIPO, 2018. Consolidated document relating to intellectual property and genetic resources. Available at: https://www.wipo.int/meetings/en/doc_details.jsp?doc_id = 393580.

Wohlfender-Bühler, D., Feusthuber, E., Wäger, R., Mann, S., and Aubry, S. J. (2016). Genetically modified crops in Switzerland: implications for agrosystem sustainability evidenced by multi-criteria model. *Agron. Sustain. Dev.* 36, 33. doi: 10.1007/s13593-016-0367-9

Yano, K., Yamamoto, E., Aya, K., Takeuchi, H., Lo, P.-C., Hu, L., et al. (2016). Genome-wide association study using whole-genome sequencing rapidly identifies new genes influencing agronomic traits in rice. *Nat. Genet.* 48, 927–934. doi: 10.1038/ng.3596

Zhang, S., Chen, X., Lu, C., Ye, J., Zou, M., Lu, K., et al. (2018). Genome-wide association studies of 11 agronomic traits in cassava (Manihot esculenta Crantz). *Front. Plant Sci.* 9, 503. doi: 10.3389/fpls.2018.00503

Zhang, X., Zhang, J., He, X., Wang, Y., Ma, X., and Yin, D. (2017). Genome-wide association study of major agronomic traits related to domestication in peanut. *Front. Plant Sci.* 8, 1611. doi: 10.3389/fpls.2017.01611

Zheng, J., Egger, C., and Lienert, J. (2016). A scenario-based MCDA framework for wastewater infrastructure planning under uncertainty. *J. Environ. Manage.* 183, 895–908. doi: 10.1016/j.jenvman.2016.09.027

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Open Source Seed, a Revolution in Breeding or Yet Another Attack on the Breeder's Exemption?

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The Open Source Seed Initiative was initiated in 2012. Following concerns about the concentration in the seed sector and the rise of patenting, the initiative is "dedicated to maintaining fair and open access to plant genetic resources worldwide in order to ensure the availability of germplasm to farmers, gardeners, breeders, and communities of this and future generations." Inspired by the debate on the anti-commons and the open source software movement, the initiative wants to create a viral system to "free" genetic resources: the use of "freed" genetic resources is made conditional to any materials derived from them being made available under the same "open source" conditions. This would be achieved under a "pledge" (in the USA) or a license contract (in Germany). The objective of this paper is to analyze whether these open source seed initiatives may deliver their goals. We compare the concept with the open innovation character of the plant breeder's rights system, exemplified by the breeder's exemption, and the major other open source initiative in the sector, BiOS. We also present other ways to limit negative impact of the patent system on plant breeding. We conclude that national sovereign rights on genetic resources may challenge the open source goals and that the German initiative may contribute to legal complexities in the seed sector. The open source movement may even contribute to the trend that openness (through the breeder's exemption) is challenged despite the intentions to the contrary. In fact, the initiatives not only free the genetic resource but also treat seeds as a common good. We question the sustainability of the business models for that approach and thus the societal benefits that can be expected from plant breeding, which may illustrate the tragedy of the commons.

Keywords: open source, Intellectual Property, Nagoya Protocol, seed system interventions, breeders rights

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INTRODUCTION

Intellectual property rights (IPR) systems have been developed in order to stimulate innovation that will serve society. Providing exclusive rights to inventors and authors provides both recognition and a basis for right holders to commercialize their intellectual assets, i.e., that users share benefits with them. The basic argument for society to grant such rather monopolistic rights is that society gets something in return. Patent applicants have to describe their invention in such a way that someone "skilled in the art" can rework it; the rights are time-bound, which means that the invention or works of art will be in the public domain at some stage. Similar to property rights at large, an important argument for such rights is the "tragedy of the commons" (Hardin, 1968), meaning that resources

are underutilized or insufficiently cared for when all have access to them and nobody takes responsibility.

Intellectual property rights were introduced in plant breeding quite recently. Apart from the Plant Patent in the USA, which is available to new varieties of many (not all) vegetatively propagated crops, such rights emerged in Europe only in the 1960s when the concept of Plant breeder's rights was introduced in a number of countries. This which spread around the world was supported by the TRIPS agreement of the World Trade Organization (WTO). Such rights relate to plant varieties only, the totality of characteristics of a certain well described group within a species. Patents on individual traits and biotechnologies entered the breeding sector only during the past three decades.

Since IPR systems should create a "quid pro quo"—a balance between the rights and the benefits for society, discussions are multiple about whether the systems (still) do that, especially when new technologies emerge such as information—and biotechnologies. The operation of IPR protection systems is under public scrutiny in various industries. Strong IPRs are claimed to cause high medicine prices, concentration of power in the Information Technology, and publishing sectors. This concern was dubbed "the tragedy of the anti-commons" (Heller, 1998), i.e., that exclusive rights may reduce innovation, or that such innovations do not reach all parts of society in a balanced way. The concerns have reached politics with the establishment of "Pirate Parties" in 38 countries with the main (or only) goal to "reform copyrights and related rights" (https://pp-international.net/about-ppi/, accessed July 2019).

Such debates may lead to either policy changes (adaptation of regulations or their implementation), or to novel uses of the rights. Open source strategies that have evolved to curb negative aspects of such exclusivity illustrate the latter approach.

This paper discusses an emerging open source movement in the plant breeding sector, dubbed "Open Source Seed." We describe the two main "Open Source Seed" initiatives and discuss them on the basis of their primary call: to "free the plant genetic resources" from corporate controls. Will the initiatives indeed open the source further or will they create other bottlenecks, both for breeders not participating in the system. The second question is whether the initiatives will be able to curb the tragedy of the commons. Will OSSI provide for sufficient innovation for society at large that requires significant investments in plant breeding to contribute to societal goals, including through more robust plant varieties, consumption qualities, and reducing food waste.

We will then compare them to existing strategies and trends that either use IPR to avoid closing off of the source, the plant genetic resources, and others that aim at changing the regulatory systems.

OPEN SOURCE SEED INITIATIVES

The OSSI-Pledge in the USA

The Open Source Seed Initiative (OSSI) was initiated in 2012 by an interdisciplinary team in Wisconsin, United States, "dedicated to maintaining fair and open access to plant genetic resources worldwide in order to ensure the availability of germplasm to farmers, gardeners, breeders, and communities of this and future generations." (OSSI, 2016). The initiative is based on the analysis that only a handful of companies account for most of the world's commercial breeding and sales of seed, and that patenting is a crucial tool in support of this trend by enhancing the power and control of these companies over the seeds and the farmers that feed the world (Kloppenburg, 2010).

Inspired by the open source software movement, OSSI wants to create a system that can go viral: initial plant materials would be freely available to breeders under the condition that the further use of any genetic resources (varieties) derived from them would be made available under the same "open source" conditions. In this way, the system would go viral up until the point that actors who would want to patent their work would not have many genetic resources left to base their breeding on—or at least that a strong parallel system would develop. OSSI specifically focuses on breeders, including farmer breeders. A difference with most open source initiatives in other sectors is these use the patent or copyright systems in order to increase openness. The holder of an IP right has the exclusive right on the commercialization of the invention (patent) or text (copyright). That right is conventionally used in a commercial setting where the IP portfolio can be a major asset of a company, but it can also serve to implement open source conditions down the chain: only users are admitted who follow the open source rules for the derivatives that they develop using the protected source material. The Intellectual Property thus allows the right holder to legally enforce such open source use. The OSS initiative in Wisconsin came to the conclusion that this would not be feasible for plant genetic resources and instead based its open source model on a non-legally-binding Pledge:

"You have the freedom to use these OSSI Pledged seeds in any way you choose. In return you pledge not to restrict others' use of these seeds or their derivatives by patents or other means, and include this Pledge with any transfer of these seeds or their derivatives." (https://osseeds.org/about/)

Even though this would not be legally enforceable, it creates a strong moral obligation. By doing that, it confirms with the opposition of the group against the increasing "juridification," i.e., the increased influence of different laws, in breeding, and seed supply. It also wants to send out a strong message to society against the patenting trend in the seed sector.

In 2014, 37 varieties of 14 species were released by various public and private breeders under the OSSI-Pledge. Since the development of varieties takes several years, it is too early to judge whether the system is going viral on the basis of these first releases. Several plant breeders, notably those operating in the organic sector, and some in US universities, have followed suit.

The OSS License—Germany

An initiative in Germany that builds on the OSSI example in the USA is taking a different approach (Kotschi and Horneburg, 2018). Where the Pledge is implemented on the basis of morality, the German initiative wants to rely on a legally enforceable bag-tag contract attached to each seed bag saying that opening the bag implies agreement with the conditions of the contract. This kind of contracts is widely used on products (shrink wrap) and

websites (clickwrap), but their enforceability depends strongly on national laws. Several non-governmental organizations have argued in the past against the use of such contracts by large seed companies to restrict the use of the seeds by farmers (Organic Consumers Association, 2010). von Gierke (2016) analyzes bag-tag licenses under German law and concludes that there are many uncertainties connected to their enforcement.

The German initiative expects to be able to identify infringements of these contracts using modern genomics techniques, and through the implementation of the Nagoya Protocol. DNA sequence data could give an indication that an open source plant has been used in the breeding process, but its predictive power likely depends on the crop and the breeding methods used. The implementation of the Nagoya Protocol in Europe obliges breeders to be able to confirm legality of the genetic resources they have used to create a new variety. Breeders thus have to keep track of their use of genetic resources and their contracts with countries from where they obtained such parent materials. The prospective use in identifying infringements of open source contracts is based on the assumption that such pedigree information will be publicly available, which is currently not the case. The OSS License was first implemented in 2017 on an existing tomato variety bred by a university, and a wheat variety bred by a biodynamic breeder. Whereas the OSSI in the USA is based on a moral call for openness, the German initiative adds additional contractual obligations for breeders and thus further contributes to the juridification processes in the seed sector.

SCOPE: OPEN SOURCE OR SEEDS AS A COMMON GOOD?

Open Source Seed claims to be an open source system for genetic resources. It does, however, not stop with making genetic resources (the source code) available for users to innovate further, but it also gives freedom to all to reproduce and sell seed of a particular variety that is available under the open source Pledge or License. Every farmer is free to reproduce a variety developed from open source germplasm and share/sell it to other growers; any seed supplier can offer the variety in the seed market. It is likely that such a seed producer can offer the same variety for a lower price than the original breeder, who has spent several years of work to develop the variety. The breeder will thus not likely recoup the years of investment needed to develop the new variety and has to have other resources to base his breeding work on. This goes beyond the concept of "freeing genetics" (Luby and Goldman, 2016) but proclaims a commons approach to seed both with breeders and farmers Kloppenburg, 2014).

The originators of the OSSI recognize that in, such a market, it will be difficult to generate profits that allow for substantial investment in plant breeding. In the USA, breeding of most crops is currently done in the public sector (the Land-Grant Universities). Even though such universities welcome income from their breeding operations just like commercial breeders, they may have good reasons to make products of their research available for free. In addition, OSSI expects voluntary contributions from seed users to provide options for sustaining breeding programs. Such payments may not be related to the agronomic benefits of the seed, but rather to their socio-political context. Luby et al. (2015) expect that contributions for "freed seed" would mirror willingness to pay higher prices for "fair trade" products. Osman et al. (2007) identify sharing responsibilities within the chain (supermarkets funding breeding) as a possible way to fund organic breeding (next to collaborating with commercial breeders). In Germany, where breeding is largely commercial, donations also—for example, through a "Saatgutfonds"[1]—support various local breeding initiatives. Such mechanisms have been developed quite recently. It remains to be seen whether they can sustain the long process of breeding.

HISTORY OF OPENNESS IN BREEDING

The Breeder's Exemption

Openness has been an important point of discussion during the early decades of scientific plant breeding. Plant breeding was not included at the time that important concepts of the national patent systems were harmonized in Paris in 1883. Farmer breeding had been going on for millennia; commercial seed production had started a century before, but systematic breeding of field crops was a new development during the latter part of the 19th century. Only after 1900, with the rediscovery of Mendel's laws on heredity, breeding developed into a science. The effects of protection of industrial inventions triggered debates by breeders especially after the first World War (Heitz, 1987). This led in the USA to the Plant Patent Act in 1930, which was only applicable to vegetatively propagated crops with the exception of edible roots and tubers. That solution for ornamentals and fruits was not considered useful in war-torn Europe where food production needed to be stimulated, and better varieties were broadly considered essential. Germany initially used the copyright system to give breeders a commercial advantage as they would be exclusively allowed to put a seal on seed bags to identify "original seed" (Heitz, 1987). All other seed producers could copy the seed, but not the seal. In the Netherlands, a small levy was charged on quantities of certified seed potatoes, which funds were distributed among the breeders according to the acreage of seed potatoes of their varieties produced (van Leeuwen, 1957). The mark-up could not be significant since such would deter the use of quality-controlled seed and as such increasing the risks of spreading potato diseases. Such levy systems have been used by producing marketing boards all over the world.

All these systems would now be considered "open source." They did, however, not provide a reasonable income to the breeder, which resulted in breeding remaining a hobby rather than a significant job, and that for the most important crops, the government took important responsibilities in many countries. Openness was, however, a major prerequisite when the IPR were discussed to support plant breeding. All *sui generis* systems that

[1]https://www.zukunftsstiftung-landwirtschaft.de/saatgutfonds/infomaterial/aktueller-infobrief-saatgutfonds/

emerged in Europe and that were harmonized in the UPOV Convention in 1961 (www.UPOV.int) explicitly avoid that the (genetic re-)source can be privatized. One of the basic concepts of plant breeder's rights is the breeders' exemption, the right of all to freely use protected varieties for further breeding. In very few countries, such as the USA, patents can be obtained on plant varieties. The patent system does not have this open innovation character. The use for breeding of a plant that falls within the scope of a patent falls under the rights of the patent holder and requires a license. Since patenting of varieties is common in the USA; it is therefore understandable that the first OSSI emerged in that country.

The plant breeder's rights systems are open with respect to the source (the genetic resource), but it does provide exclusive rights at the level of multiplication and sales of seeds of the protected variety. That rule is essential for creating a business model for plant breeding. In Europe, an estimated 15% of the sales of seed is invested in breeding. This signifies a considerable societal benefit as breeding is focused mainly on i) disease resistance as major strategy to reduce crop losses and the use of crop protection chemicals; ii) stress tolerance, currently increasingly important at the time of climate change and its associated risks for farmers; and iii) product quality, including taste and shelf life, reducing food losses.

The OSSIs extend the openness to all who want to multiply the "open source seeds." They do not only keep the source open but also give rights to those who do not innovate, but merely copy the variety. This creates additional competition in the seed market by those who have not invested in breeding similar to the situation in Europe before the variety protection systems.

Restricting Openness: Patents and Biodiversity Rights

With the developments in biotechnology, the patent system entered plant breeding. That system is rooted in the industrial business culture as opposed to the agri-cultural origins of plant breeder's rights. Patents can be granted to breeding processes and products. In most countries, essentially biological processes are exempted based on the TRIPS Agreement of the WTO (https://www.wto.org/english/tratop_e/trips_e/intel2_e.htm). Most countries, with the exception of the USA, also exempt plant varieties from patentability. However, plant traits are in most cases patentable when they meet the general patent criteria of novelty, non-obviousness/inventive step, and industrial use. The patent system does not have a breeder's exemption. Doing experiments with the invention in order to create a new commercial product requires a license of the patent holder. The holder of a patent on one trait could thus stop a breeder from using that plant for further breeding. The patenting of plant traits and its impact on the breeder's exemption worries breeders (see below).

Furthermore, countries have national sovereign rights over genetic resources as of 1993 (CBD, 1993) including crops. Countries, notably those in the so-called centers of origin (Vavilov, 1951) or centers of diversity (Hawkes, 1983) can make access to such genetic resources by breeders and researchers subject to "Prior Informed Consent" and "Mutually Agreed Terms." The Convention on Biological Diversity (CBD) (https://www.cbd.int/convention/text/) charged countries to identify national competent authorities to manage such access negotiations. Terms of such contracts may affect not only the primary user but also downstream users of the genetic resource, depending on national law. The Nagoya Protocol under the CBD (CBD, 2011) describes user obligations and charges authorities in user countries to control adherence to the contracts. An awkward thing of that Protocol is that copying a genetic resource is allowed, but innovating with it is not. These rules are getting increasingly complex with time as more and more genetic resources that breeders want to use in their crossing programs would fall under the rules.

Open innovation is, thus, not only restricted by patents but it is also increasingly challenged by biodiversity rights.

OTHER OPEN SOURCE INITIATIVES

Open source initiatives are many. The most common are open source software and open source publishing. The former includes the Linux Community (https://www.linux.org/) and the Chromium Projects (https://www.chromium.org/) inviting all to study and contribute to software improvements based on publicly available source code. These were initiated as a response to the dominance of Microsoft. The open source software initiatives keep the source code open and stimulate software developers to create solutions for particular uses. Such programs may, however, be commercialized. Open source publishing aims at the freedom to copy materials, which is quickly gaining popularity in scientific publishing. It is not the reader (or the library) but the author who is charged to cover the cost of publishing.

The breeder's rights system actually illustrates that model: the source is open and the user pays (through a mark-up on the seed price).

An initiative close to the OSSI was initiated in 1992 by the social enterprise CAMBIA (https://cambia.org/). This was an initiative by Richard Jefferson, one of the inventors of a critical component of biotechnology—the GUS-reporter system. He undertook several attempts to "democratize invention" in biotechnology, as it was considered stifled by the patent system that had grown so complex that—according to him—only few experts understand how it operates and how to decipher the treasures hidden in patents. CAMBIA developed the Patent Lens in order to increase transparency in patent landscapes (https://www.lens.org/) and worked on improving rice using new technologies. Inventions were patented and initially licensed out at very favorable terms to users working for the public good and at commercial terms to corporate users. Alternatives to the commonly used *Agrobacterium* transformation system were developed, thus bypassing the main genetic transformation patents (Broothaerts et al., 2005). BiOS, "Biology Open Source" (https://cambia.org/bios-landing/), was established as an initiative to make alternatives for every step in the modification process available under an open source license. However, this did not lead to a significant reduction in the use of commercial licenses on the *Agrobacterium* technologies. However, the initiatives did and still do impact debates on innovation in plant science.

OTHER WAYS TO LIMIT NEGATIVE EFFECTS OF PATENTS

Reduce the Scope of Patents

The patenting of plants has been a concern of many stakeholders, including the plant breeding community itself. Breeders in Europe have argued for more than a decade that the lack of a breeder's exemption in the patent system can cause serious limitations to breeders unless they are willing to spend significant resources in legal counsel by patent specialists. In 2009, the Dutch Seed Association Plantum called for an inclusion of a breeder's exemption in patent law. This triggered debates both in the breeding community, in parliaments and among legislators. The European Union decided in 2014 to include a "limited breeder's exemption" in the new Unitary Patent System. This means that breeders are free to use plant materials that contain patented traits, and only when the new variety that they develop contains that patented trait, they will need to have a license from the patent holder to commercialize the variety.

Limit Patentability

The same debate also yielded another change. The Council of EU Ministers unanimously voted in favor of a Commission Notice, interpreting the EU Directive 98/44 with the effect that patents on natural traits ("products of essentially biological processes") should not be granted (EU, 2016). Implementation of that decision by the European Patent Office proves more complex than anticipated. An attempt by the Office to implement the wish of its Council using Rule 28, exceptions to patentability is challenged at the time of writing this paper.

Patent Pools

A way to soften major negative effects of patenting, patent pools can also be a strategy. An example is the "International Licensing Platform—vegetables" (www.ilp-vegetable.org), and initiative by major vegetable-breeding companies. The agreement under the ILP is that all requests for a license have to be honored, i.e., access to a patented invention cannot be withheld by the patent holder. A referee system was put in place to determine fair license conditions when the two parties cannot conclude a contract within a given time period. It is framed as "free access but not for free." Whether this is a solution for all breeders remains to be seen.

ANALYSIS

The first important effect of the open source seed movements is that it contributes to the debate about innovation systems and the place of different types of intellectual property in search of maximizing societal benefits and minimizing monopolistic behavior. IPR have been developed in order to stimulate invention and intend to support the actual use of inventions in practical innovations that better our lives. Finding a balance between the rights and obligations of the inventor is complex in a society where quickly advancing technology increasingly puts the inventor at a distance from society at large.

An important question would therefore be whether doing away with such rights would result in more and better innovations. Could public funding provide the foundation for all plant breeding? Or could alternative funding mechanisms provide sufficient funds sustainably, which is required to develop better varieties of all different crops for the diversity of farming systems and for a quickly changing society? Lammerts van Bueren et al. (2018) and Kotschi and Wirz (2015) identify the challenge and suggest a combination of public and chain partner (through foundations) funding. Looking at the vast investments made in plant breeding—in the Netherlands vegetable-breeding sector alone, conservatively estimated at 300 million Euro per year—it may be doubted that the same intensity of breeding could be sustainably supported through such funding mechanisms. Here, it is important to identify the difference between the concept of "open source," which applies to the use of genetic resources, and "commons" which also relates to the use of seeds. The literature on the subject does not make that distinction. The OSS initiatives highlight the former but appear to pursue the latter.

Another effect of the open source license is likely, in which when it would operate side-by-side commercial breeding, it would add again to limiting the breeder's exemption. A breeder who operates in the business models of the open innovation system created by breeder's rights could not "touch" any material under the OSS license without challenging his freedom to protect the new varieties that he would produce. The trend created by patents and biodiversity rights of limiting access by breeders to the genetic diversity that they need to breed better varieties would be attacked from yet another side. Openness can thus limit access to genetic resources just like patents and biodiversity rights. Initiatives that simply do not apply for patents or breeder's rights (Wirz et al., 2017) would not have such negative side effects. Such public domain approaches are not popular in the open source literature as it may invite others to appropriate "derivatives" (Luby et al., 2016).

Alternative ways to rebalance the rights with the benefits of society through regulatory change require significant time. This is likely less when implementing rules are changed compared to adapting the laws themselves. Rebalancing through voluntary measures by right holders themselves has the disadvantage that not all parties may join. From an open source perspective, the breeder's rights system creates no issues.

CONCLUSION

"Open Source Seed" responds to an ongoing debate in society about the provision of IPR that, on the one hand, aim at supporting innovation or creative works, but that also risks to stifle the same through its exclusive rights.

It is understandable that the OSSI emerged in the United States, where patenting of plant varieties is common, and internationally agreed rights on biological diversity are not valid. The USA is unique in this legal position.

If the movement is also meant to oppose the "juridification" of plant breeding, then the OSSI-Pledge used in the USA is a more logical, but legally less strong, solution that the OSS license proposed in Germany.

If it is the intent to create openness toward genetic resources, then the breeder's exemption in the plant breeder's rights system, which is the dominant protection system in almost all countries already, fulfils these needs. When, however, it is not only the intent to protect the (genetic re-) source but also to allow everybody to compete in the seed market with breeders, then the name "open source" is a misnomer. Then, the initiatives may be better framed under the concept of the Commons. But that term would contradict the effect that the OSS Initiative, at least the one operating through the license system, can reduce access to genetic resources by conventional plant breeders in their business model.

There are alternative ways to limit the impact of patent rights, i.e., by rebalancing the patent system itself and by avoiding strategic (monopolistic) use of the rights through patent-pool type of agreements. Neither these, nor the open source seed initiatives, can reduce the negative impact of biodiversity rights on the openness of genetic resources for plant breeding.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

REFERENCES

Broothaerts, W., Mitchell, H. J., Weir, B., Kaines, S., Smith, L. M., Yang, W., et al. (2005). Gene transfer to plants by diverse species of bacteria. *Nature* 10 (433), 629–633. doi: 10.1038/nature03309

CBD. (1993). Convention on biological diversity https://www.cbd.int/convention/text/ (accessed 14.07.2019).

CBD. (2011). *Nagoya Protocol on access to genetic resources and the fair and equitable sharing of benefits arising from their utilization to the convention on biological diversity*. Montreal: Secretariat of the CBD, 25 pp. https://www.cbd.int/abs/doc/protocol/nagoya-protocol-en.pdf (accessed 14.07.2019).

EU. (2016). Commission notice on certain articles of Directive 98/44/EC of the European Parliament and of the Council on the legal protection of biotechnological inventions (2016/C 411/03). Official Journal of the European Union, 08.11.2016. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52016XC1108(01)&from=EN (accessed 14.07.2019).

Hardin, G. (1968). The tragedy of the Commons. *Science* 162 (3859), 1243–1248. doi: 10.1126/science.162.3859.1243

Hawkes, J. G. (1983). *The diversity of crop plants*. Cambridge, Mass: Harvard University Press, 184 p. doi: 10.4159/harvard.9780674183551

Heitz, A. J. L. (1987). *The first 25 years of the international Convention for the Protection of New Varieties of Plants*. UPOV Publication no. 879(E): Geneva, 134 p.

Heller, M. A. (1998). The tragedy of the anticommons: property in the transition from Marx to markets. *Harv. Law Rev.* 111 (3), 621–688. doi: 10.2307/1342203

Kloppenburg, J. (2010). Impeding dispossession, enabling repossession: biological open source and the recovery of seed sovereignty. *J. Agrarian Change* 10 (3), 367–388. doi: 10.1111/j.1471-0366.2010.00275.x

Kloppenburg, J. (2014). Re-purposing the master's tools: the open source seed initiative and the struggle for seed sovereignty. *J. Peasant Stud.* 41 (6), 1225–1246. doi: 10.1080/03066150.2013.875897

Kotschi, J., and Horneburg, B. (2018). The Open Source Seed License: a novel approach to safeguarding access to plant germplasm. *PLoS Biol.* 16 (1), 2018. doi: 10.1371/journal.pbio.3000023

Kotschi, J., and Wirz, J. (2015). Wer zahlt für das Saatgut? Gedanken zur Finanzierung ökologischer Pflanzenzüchtung. Arbeitspapier. AGRECOL und Sektion für Landwirtschaft. Marburg und Dornach. http://www.agrecol.de/files/Kotschi_&_Wirz%20Engl_12_05_15.pdf (accessed 14.07.2019).

Lammerts van Bueren, E. T., Struik, P. C., van Eekeren, N., and Nuijten, E. (2018). Towards resilience through systems-based plant breeding. A review. *Agron. Sustain. Dev.* 38, 42. doi: 10.1007/s13593-018-0522-6

Luby C. H., and Goldman, I. L. (2016). Freeing crop genetics through the open source seed initiative. *PLoS Biol.* 14 (4), e1002441. doi: 10.1371/journal.pbio.1002441

Luby, C. H., Kloppenburg, J., and Michaels TE and Goldman, I. L. (2015). Enhancing freedom to operate for plant breeders and farmers through open source plant breeding. *Crop Sci.* 55, 2481–2489. doi: 10.2135/cropsci2014.10.0708

Organic Consumers Association (2010). Millions against Monsanto. Companies put restrictions on research into GM crops. https://www.organicconsumers.org/news/companies-put-restrictions-research-gm-crops (accessed 14.07.2019).

Osman, A. M., Müller, K.-J., and Wilbois, K.-P. (Eds), (2007). Different models to finance plant breeding. Proceedings of the ECO-PB International Workshop on 27 February 2007 in Frankfurt, Germany. Driebergen/Frankfurt European Consortium for Organic Plant Breeding, 33 pp. https://www.eco-pb.org/fileadmin/eco-pb/documents/reports_proceedings/proceedings_070227.pdf (accessed 14.07.2019).

OSSI (2016). The Open Source Seed Initiative. https://osseeds.org/ (accessed 14.07.2019).

Van Leeuwen, J. C. (1957). De ontwikkeling van het kwekersrecht. (*the development of plant breeder's rights*). Pp132-150 in: "Tussen ras en gewas. Een serie artikelen opgesteld ter gelegenheid van het 25 jarig bestaan van de NAK". NAK - Wageningen. (in Dutch).

Vavilov, N. I. (2016). *The origin, variation, immunity and breeding of cultivated plants* (Leydon: translated by K. Starr Chester). Vol. 13. Chronica Botanica, 1–366.

von Gierke, K. (2016). Bag tag (licence) agreements. Things to know under German Law.https://www.nortonrosefulbright.com/en/knowledge/publications/d0d36acc/bag-tag-licence-agreements (accessed 14.07.2019).

Wirz, J., Kunz, P., and Hurter, U. (2017). Seed as a commons. Breeding as a source for real economy, law and culture. Assessment and future perspectives for non-profit seed and breeding initiatives. Goetheanum, Dornach & Fund for Crop Development, Feldbach, Switzerland. https://www.sektion-landwirtschaft.org/fileadmin/SLW/Literatur/Saatgutstudie/seeds_as_a_commons.pdf (accessed 14.07.2019).

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Balanced Options for Access and Benefit-Sharing: Stakeholder Insights on Provider Country Legislation

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The over-arching aim of the access and benefit-sharing (ABS) of genetic resources is to enable fair distribution of benefits between the users (such as universities and biotech companies) and providers (such as biodiversity rich countries) so as to both open the doors for innovation and create incentives for biodiversity conservation. Access to genetic resources is crucial for research related to conservation of plant genetic resources as well as R&D for agricultural products and evolved crops that can attain to the new weather conditions climate change brings. Therefore, access to genetic resources in general as well as benefit-sharing from that access is a key element for sustainable development in order to secure research as well as environmental sustainability and resource availability. ABS is currently a rapidly developing and evolving field that is shaped by each and every implementation of the Parties. This means that the national implementation of the Parties determine how ABS goals are realised and how ABS principles find form within regulatory mechanisms. These principles are found in international legal documents such as the Convention on Biological Diversity (CBD) as well as Nagoya Protocol. Additionally, decisions and guidelines drafted by the Conference of the Parties to the Convention on Biological Diversity shape these principles that are then to be fulfilled by the Parties when drafting their ABS laws by means of implementing regulatory mechanisms that comply with the international law. This article reviews 20 provider country's ABS frameworks as well as one regional law with the aim of identifying the common regulatory mechanisms that find place in these legal texts. This descriptive approach is then followed by an empirical comparative analysis through semi-structured stakeholder interviews in order to identify the most beneficial regulatory mechanisms according to ABS experts that belong in four different stakeholder groups (provider countries, academic users, industrial users and collections)

Keywords: access and benefit-sharing, Nagoya protocol on access to genetic resources and the fair and equitable sharing of benefits, genetic resource, natural product research, utilization

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INTRODUCTION

Access and benefit-sharing (ABS) is a system under public international law that aims to fairly distribute benefits arising from genetic resources between the users of genetic resources (such as universities and biotech companies) and provider countries (regulatory authorities in biodiversity-rich countries). It is a system that finds its basic principles within the Convention on Biological Diversity (CBD) (United Nations Convention on Biological Diversity, 1992). These principles are

further specified within the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (Nagoya Protocol, 2011). The CBD and the Nagoya Protocol, together with the decisions of the Parties thereof, establish the international ABS goals. These goals have been explored in a previous study by the author (Sirakaya, 2019).

ABS is a rapidly evolving field that is shaped by the implementation of the Parties to the CBD and the Nagoya Protocol. This means that the national implementation of these countries determines how ABS goals are realized and how ABS principles find form within regulatory mechanisms. These principles have to be implemented by the Parties when drafting their ABS laws by means of putting regulatory mechanisms in place which are in line with the international ABS goals. In other words, how provider countries regulate ABS directly shapes the way ABS principles are implemented.

This article reviews 20 of these national ABS laws and a regional ABS law implemented by provider countries throughout the world with the aim of describing the different types of regulatory mechanisms that provider countries use and providing examples of some of the countries that utilize them. This descriptive approach is then followed by an empirical comparative analysis through semistructured stakeholder interviews to identify the approach toward various mechanisms on access, benefit-sharing, and compliance of ABS experts that belong to four different stakeholder groups (provider countries, academic users, industrial users, and collections).

METHODOLOGY

The methodology of this article consists of two stages. The first stage follows a descriptive approach in reviewing and explaining common regulatory mechanisms on ABS. Within this stage, a legal analysis of primary sources (national legislation, regulations, policies, and guidelines where applicable) within selected countries and regions is conducted to explore the commonalities and differences provider countries have in regulating ABS matters. Once identified, these regulatory mechanisms are briefly described and explained. The explanation is then followed by a comparative analysis of the selected countries' and region's related regulatory mechanisms regarding on access, benefit-sharing, and compliance.

The second stage follows an empirical approach to discover and analyze the stakeholder perception on these previously identified common regulatory mechanisms on ABS. A qualitative analysis in the form of semistructured interviews is conducted for acquiring stakeholder perceptions on these mechanisms, as well as for demonstrating the qualitative data on stakeholder perceptions on them.

The purpose of this article is not to fully describe these 21 legal documents in detail but rather identify common regulatory elements and subjects them to stakeholder interviews.

The choice of the countries subject to this review study is made based on the following criteria:

- Richness in biodiversity
- Diversity in terms of economic development
- Diversity in terms of maturity of the ABS framework
- Diversity in signatory status under the Nagoya Protocol[1]

The selection furthermore aims to demonstrate a worldwide approach as there is at least one country in each continent that has a state/region with an ABS framework. After applying these criteria, the following ABS frameworks have been selected for review: Andean Community, Australia, Brazil, Costa Rica, Dominican Republic, France, Ecuador, Ethiopia, India, Japan, Kenya, Malaysia, Namibia, Norway, Philippines, Republic of Korea, South Africa, Spain, Thailand, Uganda, and Vietnam.

Looking into regulatory issues related to ABS, the author has identified four key stakeholders: the government (as the provider), collections, academic users, and industrial users. These have been identified in line with Freeman's definition of stakeholder, which is "any group or individual who is affected by or can affect the achievement of an organization's objectives" (Freeman and Mcvea, 2001). These key stakeholders' involvement in the regulatory processes is vital to form an ABS system that is effective and efficient and that attains the international ABS goals (Swiderska, 2001).

OPTIONS IN ACCESS AND BENEFIT-SHARING

With the aim of compiling the international ABS principles regulated under the CBD and the Nagoya Protocol with additions from various COP Decisions, the author has previously conducted the review of these international documents on ABS and compiled 11 ABS goals that are prescribed by these documents that are then to be fulfilled by the Parties through their national ABS frameworks. These goals found through the literature review conducted by Sirakaya (2019) are listed as follows:

1) Predictable conditions (Nagoya Protocol Preamble)
2) Legal certainty (Nagoya Protocol Article 6, COP Decision V/26, VII/19, VIII/4)
3) Transparency (Nagoya Protocol, COP Decision V/26)
4) Fairness and equity in negotiations (Nagoya Protocol, COP Decision V/26)
5) Sustainable use of biodiversity components (CBD Article 1, Nagoya Protocol Preamble, Article 8, Article 9, COP Decisions V/26 and VII/19)
6) Cost-effective measures (Nagoya Protocol Article 6, COP Decisions VII/19, VIII/4)
7) Scientific research based on genetic resources (CBD Article 15.6)
8) Strengthening the ability of indigenous people and local communities to benefit from the use of traditional knowledge

[1]All of the selected countries are parties to the Convention on Biological Diversity, yet some of them have not yet ratified the Nagoya Protocol.

(Nagoya Protocol Articles 5, 6, 7, 12, 21, 22, COP Decision V/26, VI/24)
9) Tech transfer and cooperation to build research and innovation capacity in developing countries (Nagoya Protocol, COP Decisions VIII/4, VII/19, VI/24, V/26)
10) Creating incentives to conserve biodiversity (CBD Article 11, COP Decision VI/24, Nagoya Protocol Preamble)
11) Innovative solutions for transboundary situations (Nagoya Protocol Preamble and Article 11)

In principle, provider countries' national ABS frameworks should aim to attain these goals by means of implementing regulatory mechanisms that aid these goals' principles. However, provider countries can significantly differ in their approaches when enacting provisions related to ABS of genetic resources. Furthermore, there exists no consensus regarding the state practice at the regulatory level. This is because some countries choose to enact specific laws on ABS, whereas some regulate ABS-related issues under framework legislation related to the environment or biodiversity or modify existing legislation to include ABS obligations. Nevertheless, similarities can be found with regard to the regulatory options that provider countries implement within the field of ABS. After analyzing 20 provider country approaches as well as one regional approach toward ABS, this section compiles the most commonly used regulatory options within the ABS frameworks of the provider countries into categories of regulatory mechanisms, such as material scope (what type of genetic resources are regulated), temporal scope (when can the ABS obligations be triggered), activity scope (which activities are regulated), geographical scope (within national laws, this comes up when regional competence or competence based on the type of genetic resource is divided), and other types of mechanisms found through the review of primary sources (i.e., country legislation on ABS), such as the requirement for an access permit (3.1.), requirement for a benefit-sharing agreement, standardized or negotiable conditions, types of monetary and non-monetary benefit-sharing found within the ABS frameworks (3.2.), and provisions on compliance and monitoring (3.3.) (**Table 1**).

Access

It should first be noted that neither the CBD nor the Nagoya Protocol defines access to genetic resources. Furthermore, the countries subject to this study either do not define access or define it in accordance with their understanding of access. Therefore, this study refrains from defining access and claiming either approach as the aim of this study is to point out the common elements in national regulatory options on ABS.

Options for Material Scope

- *In situ* access only: A permit or notification is only required when access happens within the geographical borders of the provider country. This is the classical access case foreseen by the CBD, where a researcher takes a sample of a genetic resource in a field/forest/nature reserve/public or private land (CBD.int, 2011).
- *In situ* and *ex situ* access: A permit or notification is required when access happens within the geographical borders of a provider country as well as through biodiversity biobanks, which are collections of biological samples that are held for preservation, research, and/or conservation purposes (e.g., genebanks, botanical gardens, natural history museums) (Shaw et al., 2014). Some frameworks (e.g., Brazil, 2015) enable the law to apply retroactively, by choosing to include the genetic resources accessed before their legislation came into force, within the scope of their ABS framework. This means that the material found in collections that were accessed before the enactment of the law would still require permit from the competent authority of the provider country. Other countries choose not to apply such retroactive provisions and only regulate the access that happens after the date of entry into force of their national ABS framework.
- *In situ*, *ex situ*, and access to digital sequence information (DSI): Both physical accesses, access through biobanks (i.e., collections) and access to DSI, are covered. DSI is not defined under the international legal sphere. It has been introduced to the Parties to the CBD and Nagoya Protocol during COP 13 UNEP (2016a, 2016b). Parties to the Convention are currently discussing the possible inclusion of access to or use of DSI within the scope of the CBD and the Nagoya Protocol (Laird and Wynberg, 2018). For instance, the Andean Community (1996) includes DSI within the scope of application.

Options for Mechanism to Trigger Access (Temporal Scope)

- Access for sampling: The access requirements are triggered before the material is sampled *in situ* or obtained from an *ex situ* source. In this case, the obligations come into place at the moment the user obtains the ability to perform R&D activities on the genetic resource. The obligations are triggered prior to performing these activities. Kenya (2006, 2013) follows this approach.
- Access for utilization: The access requirements are triggered after the user obtains the ability to perform R&D. The trigger here is not the physical access, which enables the user to conduct R&D activities, but rather the utilization activity itself. This is the approach taken by the Dominican Republic (2018) as it excludes the access of genetic resources by *ex situ* collections, solely for conservation purposes and not for utilization or third-party transfer. Brazil (2015) is another example of a country that does not place the trigger on access but rather on utilization.
- Access to a previously utilized genetic resource for new utilization: The requirements are triggered when a new utilization activity occurs to a genetic resource that was previously made available to the user. France (2016) explicitly mentions this in its legal framework.

TABLE 1 | Commonly used regulatory options on access and benefit-sharing.

Commonly used regulatory options on ABS				
	Access	Scope	Material scope	*In situ* only *In situ + ex situ* Access to DSI
			Temporal scope	Sampling Utilization Access to a previously utilised genetic resource for new utilisation
			Utilization scope	Research Development R&D
		Pre-condition for access		Mandatory BSA Voluntary BSA
		Options for regulatory mechanisms		Permit Notification
		Standardisation		Standardised Case-by-case
	Benefit-sharing	Types	Monetary	Joint ventures Access fee Up-front payment License fee Royalties Salaries and funding Trust fund payment
			Non-monetary	Raw data Research results Capacity building Technology transfer Research directed towards priority needs of the provider country Food and livelihood security benefits
		Trigger		Access Utilisation
		Standardisation		Standardised Case-by-case
		Renegotiability		Renegotiable when the user and/or the intent changes Non-renegotiable
	Compliance	Sanctions		Administrative fines in any case of breach Criminal sanctions in any case of breach Administrative fines for light breach, criminal sanctions for severe breach

It is crucial to keep in mind that having utilization as trigger for access does not necessarily mean that all of the genetic resources accessed prior to the enactment of the national laws are within the scope of ABS obligations.

Options for Utilization Scope

- Research: Access for research activities only. The access is only permitted for activities that do not involve any product/process development.
- Development: This refers to access for product/process development.
- Research and Development (R&D): Access for both research and development.

Here, it should be noted that the division between research and development is yet to be clarified. While the vast majority of the countries regulate R&D on genetic resources (e.g., Brazil, 2015), some countries (such as Ethiopia and Thailand) do not include this distinction or define these differences.

Benefit-Sharing Agreement as a Condition of Access

- Mandatory benefit-sharing agreement: This stipulates that a benefit-sharing agreement is to be signed between the provider and the user prior to access. This is the approach taken by France (2016), Thailand (2011), and Vietnam (2017).
- No mandatory benefit-sharing agreement, which means that there is no obligation to enter into a benefit-sharing agreement prior to access, yet this obligation may arise during different stages of R&D. Japan and the Republic of Korea do not require a benefit-sharing agreement prior to access.

Options for Regulatory Mechanisms

- Notification-based access: The user is to provide information regarding the modalities of access (defining material and

temporal scope, persons/entities involved, transfer, intent, access and/or utilization) to the competent authority. However, in this case, the user can proceed with the activity without waiting for a response. Here, the notification would not qualify as a permit because a permit requires the applicant to wait for the authorization of the competent authority to commence its activities. The Republic of Korea (2017, 2018) is one of the countries that only requires notification to the competent authority regarding access.

- Permit-based access: Users who want to access a genetic resource must apply for access and wait for authorization prior to proceeding with their activities. This is referred to as the Prior Informed Consent (PIC) under Article 6 of the Nagoya Protocol. The majority of the countries have this as a regulatory mechanism for access.

Granting Authority

- Centralized, single institution, a one-stop-shop to go for the applicant: This is the case where only one authority or institution (e.g., a ministry, a research institute, a university, or an independent institution) has the competence for the entirety of the country and all types of genetic resources. The majority of the countries subject to this study have a centralized, single institution mandated to grant access to genetic resources.
- Several institutions mandated either according to the types of genetic resources or due to regional competence regarding genetic resources: In some cases, several regions may have their competence on the issues related to genetic resources from that region. This is especially the case for federal states. In addition, some states choose to have multiple competent authorities based on different types of genetic resources. For instance, the Ministry of Environment may be mandated to deal with genetic resources accessed from national parks, whereas the Ministry of Agriculture may be mandated for plant and animal genetic resources. Thailand (Thailand, Office of Natural Resources, Environmental Policy and Planning, 2014) is one of the countries that have several competent authorities depending on the type of genetic resource, whereas Spain (2007) has numerous competent authorities due to regional competence.

Standardized or Case by Case

- Standardized access conditions prescribed by law, regulations, and/or polices: Some countries choose to have PIC as a standard contract with predefined terms and conditions for access, often accessible through the annexes of the ABS law, the regulation, or online. Some countries, such as India, (2014), Spain (2007), South Africa (2008), and the Philippines (2005), on the other hand, specify the minimum content of the PIC within their ABS frameworks.
- Case-by-case conditions depending on the type of access and type of genetic resource: Some countries choose to have general principles within their regulatory framework on ABS, yet draft a unique, bilateral PIC document for each case. In some cases, the information required from the applicant is prescribed by law; in other cases, the applicant has to contact the competent authority to find out what documents are necessary for the case in hand. The majority of the countries tend to favor case-by-case negotiation in their national laws.

Mandatory Local Partner

- The user must apply for a permit with a local public or private partner, or the local partner has the responsibility to obtain and manage the permit. This local partner can be a university, a company, a nongovernmental organization, which, in theory, helps the user obtain legal certainty and takes part in the R&D activities on the genetic resources subject to the benefit-sharing agreement. The Philippines, for instance, is one of the countries that require a local partner.
- The user can apply for a permit without a local partner. This is the approach taken by France and Spain.

Facilitated Access for Non-Commercial Research

- Yes, non-commercial research is subject to favorable access conditions compared to commercial research. Favorable access conditions can be exemplified as simplified ABS systems for non-commercial research, where fewer documents are required from the applicant, a permit is given in a shorter time frame, or where benefit-sharing is done on non-monetary and/or voluntary basis. Australia (2012a), Spain, South Africa, and Thailand are some of the countries that have favorable access conditions for non-commercial research. Ecuador (2011), on the other hand, provides the option of framework contracts for non-commercial research.
- No, both commercial and non-commercial research is subject to the same conditions. Kenya follows this approach.

Options to Renegotiate ABS Contracts

- Renegotiation when the user changes: In the cases where a user transfers the genetic material to a subsequent user who is not a party to the contract between the user and a provider country, nor it is mentioned in the PIC that third-party transfer is allowed, the new user must obtain a new PIC either before or after it receives the material from the previous user.
- Renegotiation when the intent changes: In the cases where a user's scope of activity regarding the genetic resource accessed from the provider country shifts from non-commercial to commercial research and where the PIC does not allow such research activity, the user is to then renegotiate the PIC conditions with the provider country before or after the commercial research activity begins.

For instance, Vietnam explicitly specifies both of these options.

Benefit-Sharing

The explanation below categorizes benefit-sharing types as follows. Non-monetary and monetary: Based on whether the user pays benefits in monetary value or in actions.

- Mandatory and voluntary: Based on the government's choice on making the benefit-sharing mandatory or voluntary for the user.

Non-monetary Benefit-Sharing

- Raw data: This type of data could pertain to the core information on genetic resource related to its phenotypic characteristics. Ethiopia (2006) foresees this type of benefit-sharing as a part of the obligations foreseen for the access permit holder.
- Sharing of research results: There is no indication on what research results mean. However, following the daily practice of research institutions, we could conclude that this would be the reports that describe the results of a research based on its methodology (Anderson, 2003). The user would then need to provide a report as part of the non-monetary benefit-sharing obligation. Some countries, such as Australia (2012b), and India, further explain which research results would be of interest to them.
- Capacity building: At the international level, capacity building (or capacity development) is defined as "any intervention or activity purposely designed to contribute to the development or strengthening of the capabilities of people, institutions and systems" (CBD.int, 2019; UN.org, 2019). Article 22/4 of the Nagoya Protocol includes the following categories within the scope of capacity building:
  a) Capacity to implement, and to comply with the obligations of, this Protocol;
  b) Capacity to negotiate mutually agreed terms;
  c) Capacity to develop, implement, and enforce domestic legislative, administrative, or policy measures on access and benefit-sharing; and
  d) Capacity of countries to develop their endogenous research capabilities to add value to their own genetic resources.

In addition, Article 22/5 further explains which actions would fall within the scope of these categories.

While some countries only mention capacity building as part of the non-monetary benefits (e.g., Australia; France (2017); and Kenya), some countries, such as South Africa (2008) and Uganda (2005), follow a more specific approach by including some of the capacity-building activities mentioned under Article 22/5 of the Nagoya Protocol.

- Technology transfer: Referring to Articles 15, 16, 18, and 19 of the CBD, Article 23 of the Nagoya Protocol obliges Parties to "undertake to promote and encourage access to technology by, and transfer of technology to, developing country Parties, in particular, the least developed countries and small island developing States among them, and Parties with economies in transition, in order to enable the development and strengthening of a sound and viable technological and scientific base for the attainment of the objectives of the Convention and this Protocol." Some countries, such as Costa Rica (1998), take an approach where technology transfer is a state obligation embodied in the ABS framework, which means that when negotiating benefits, the state is obliged to seek out technology transfer options. Most countries, however, merely list technology transfer as a type of non-monetary benefit-sharing (e.g., Ethiopia, Kenya, and Vietnam). Some countries, like the Philippines (2005), include the terms and conditions of technology transfer in their standard ABS contracts. Ecuador's ABS Framework obliges the parties to discuss technology transfer options during benefit-sharing negotiations.
- Research directed toward priority needs: The Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization (UNEP, 2002) includes this as a type of non-monetary benefit-sharing and exemplifies them as research related to health and food, taking into account domestic uses of genetic resources in provider countries. Some countries, such as India and Namibia (2017), list this non-monetary benefit-sharing option in their ABS frameworks. Australia refers to the Bonn Guidelines in their model benefit-sharing agreement.
- Food and livelihood security benefits: This category is also mentioned under the Bonn Guidelines. It is not defined what it covers nor what is entails. Yet, some countries (e.g., India, Uganda, and Vietnam) include this type of benefit within their list benefits.

Monetary Benefit-Sharing

- Joint Ventures: This Concept Is Not Defined Under the CBD or Its Nagoya Protocol, Yet the Organisation for Economic Co-operation and Development (OECD, 1993) Provides Us With the Following Definition: "A Joint Venture Is an Association of Firms or Individuals Formed to Undertake a Specific Business Project." Most of the Countries Subject to This Study (E.G., Kenya, Namibia, Brazil, and India) Refer to Joint Venture as an Option for Monetary Benefit-Sharing and Do Not Oblige Parties to Enter Into Such Agreements.
- Access fee/fee *per* sample: This type of benefit-sharing occurs when the access obligations are triggered more as an administrative fee either *per* applicant or *per* sample. Today, some countries (e.g., Kenya and Namibia) only mention such an option as a type of monetary benefit-sharing within their ABS frameworks, whereas some countries (such as Malaysia, 2017; Vietnam) indicate the types of fees or sometimes the amount of fees (India; South Africa, 2012; the Philippines; Uganda, 2007) payable prior to access.
- Up-front payments: This concept was initiated in Costa Rica through the access-for-fee agreement between the National Biodiversity Institute (INBio) and the pharmaceutical company Merck (Sittenfeld and Gamez, 1993). The concept got furthermore enshrined in the Bonn Guidelines. This type of benefit-sharing occurs when the user pays not only for the access fee but also for the negotiated amount of benefit-sharing before utilization. Some of the countries, such as India, Namibia, Kenya, and Uganda, list up-front payments as a monetary benefit option within their ABS frameworks.
- License fee: There is no unified definition of license fees within the field of ABS; however, this type of payment is rather common in the field of intellectual property law. According to the World Intellectual Property Organization

(WIPO), a licensing agreement is a partnership between an intellectual property rights owner (licensor) and another who is authorized to use such rights (licensee) in exchange for an agreed payment, which either comes across as royalties or license fees. Royalties are usage-based payments, whereas license fees often occur periodically (World Intellectual Property Organization, 2004). License fees have been used within the field of ABS on several cases. Most of the countries (e.g., Uganda, India) mention this as a type of monetary benefit option within their frameworks.

- Royalties: Royalties are usage-based payments made by the user of a genetic resource to the provider country. They are often agreed to as percentages of gross or net revenue. Percentages of royalty payments are foreseen both in the Brazilian and Costa Rica (2003) ABS systems. The Dominican Republic is one of the countries that mention this as a monetary benefit-sharing option.
- Salaries and research funding: The majority of the provider countries' ABS frameworks (e.g., Namibia, Kenya, Uganda, and Ethiopia) have this included as a benefit-sharing option. Although some of them include this under non-monetary benefit-sharing, the performance of this act only requires the transfer of a monetary amount and thus is suited better as a monetary benefit option.
- Trust-fund payment: This is a type of benefit-sharing payment made directly to a fund foreseen under the national ABS framework. The current ABS Framework in South Africa foresees compulsory payment to be made to the Bioprospecting Trust Fund after concluding the benefit-sharing agreement.

Some countries, such as Vietnam, list various benefit-sharing options without differentiating between their monetary and non-monetary character. Here, it should also be noted that some of the benefit-sharing options that can be found under the Bonn Guidelines are not included here as they did not exist in the majority of the ABS frameworks within the countries that have been sampled in this study.

When Will Benefits be Transferred/Trigger for Benefit-Sharing

- At the point when access obligations have been triggered: This is the case for countries that oblige up-front payments, access fees, or fees *per* sample. The user is then to pay such fee prior to or within a specified period after the signing of the PIC.
- At the point of utilization: In this case, the user shares the negotiated or predetermined amount or performs the activity subject to the agreed non-monetary benefit during the R&D process.

India foresees both these options depending on the activity.

- At the point of commercialization: Most countries' approach to benefit-sharing agreements is to negotiate a trigger that is tied to the commercialization of the product. Alternatively, some countries explicitly mention that they expect benefit-sharing at this stage. This option automatically comes across for countries that laid down obligations for users to pay license fees. Nevertheless, Brazil also follows this approach, despite having enacted the mechanism of royalty payments.
- At the point (or a specified period after) the user or provider receives first benefits from the utilization of genetic resources (GR): The user only benefits (in monetary terms) from the utilization only sometime after a product or a process developed through the utilization of genetic resources is finalized and released into the market. This fact is considered in Brazil as the Brazilian ABS Framework foresees the payment of 1% of annual net revenue.
- Payment tied to the application of or exploitation of intellectual property (IP) rights: This also comes across as milestone payments. Milestone payments are the type of payments in licensing agreements where the payment is triggered by an activity or occurrence of an event (Crama et al., 2009). In its model benefit-sharing agreement, Australia (2012), takes the exploitation of IP rights into account when establishing the trigger for benefit-sharing.

Exemption From Benefit-Sharing

- Exempting the user from benefit-sharing for certain types of use (e.g., no benefit-sharing needed when the utilization is directed at biodiversity conservation, food security): For example, India exempts collaborative research projects (subject to approval by the competent authority) as well as non-commercial utilization for publication purposes from benefit-sharing. In addition, Norway (2016) exempts private and non-commercial users from obtaining PIC and MAT for utilizing traditional knowledge associated with genetic resources.

Preset Conditions Versus Case-By-Case Negotiation

- Preset: Benefit-sharing conditions and triggers are set within the law, regulations, and/or policies. The user signs a standard contract drafted by the provider country. Australia's ABS framework includes a model benefit-sharing agreement, whereas Indian ABS Guidelines specify the amount of monetary benefits to be shared in specific situations. On the other hand, the Brazilian ABS framework specifies the percentage of the benefit to be shared based on the annual net revenue obtained from a finished product or a process.
- Case-by-case negotiation: Benefit-sharing is subject to negotiation between the providers and users. The majority of the countries in this study (e.g., Kenya, South Africa, Thailand, France, Spain, and Costa Rica) have ABS frameworks that lead to case-by-case negotiation for access permits.

Compliance

Sanctions

- Administrative fines in any case of breach
- Criminal sanctions in any case of breach

The Philippines foresees both administrative fines and criminal sanctions.

- Administrative fines for light breach, criminal sanctions for severe breach (misappropriation/intentional breach/repetitive noncompliance): This is the case for the Republic of Korea.

Other than sanctions, some countries have monitoring requirements to ensure compliance. For instance, Thailand obliges annual reporting throughout the R&D process, whereas Brazil requires notification prior to commercialization. However, since these options were not taken on by the majority of the countries subject to this comparative study, the options did not make it to the interviews.

INTERVIEWS

The stakeholder survey conducted in an initial study by the author (Sirakaya, 2019)[2] included a question on the participant's availability for an in-depth interview regarding ABS options. Fifty-three of the respondents demonstrated their interest, and 20 ended up participating to the interview. The distribution of the participants among the stakeholder groups has proven to be rather homogeneous as five experts represented provider countries, six experts represented (public) collections, five represented industrial users (from various sectors, such as agriculture, pharmaceuticals, and industrial biotechnology), whereas four represented academic users (postdoctoral researchers and professors associated with various universities). Written informed consent forms were obtained from all of these experts.

The stakeholder interview has been designed in a semistructured manner. The questions on access and compliance asked stakeholders to rank the preference *per* regulatory option (**Table 2**) on a scale of 1 to 3, with 1 being the most favorable and 3 being the least favorable. The questions on benefit-sharing asked the stakeholders to rank the impact (from very positive to very negative) and burden (from burden to very heavy burden) of engaging in the given monetary or non-monetary option.

Perceptions on Access

Question 1 was regarding the contact information of the stakeholders. Except for one participant, all of the interviewees representing provider countries were a part of the regulating body. Two of the provider country representatives were based in Africa, and the rest were scattered around the world. Participants representing collections were mostly based in the policy division of the collections they represented. All of the interviewees representing industrial users and academic users were based in either Europe or North America.

Due to the confidentiality concerns of the majority of the participants, the names of the interviewees will not be published.

[2]The survey has been sent to over 600 stakeholders including all of the national competent authorities of parties to the CBD, all of the national focal points, academic institutions, collections, and industrial users worldwide. The selection of the stakeholders is based on their function in their institution as well as their demonstrated interest in ABS (published articles, their position and expertise, attendance to conferences, workshops, or discussions related to ABS). Two hundred twenty responses were obtained.

Question 2 asked stakeholders to rank material scope options. The majority of the stakeholders opted for ABS frameworks to cover *in situ* and *ex situ* access, whereas the least favorable option stated by the majority of the stakeholders was *in situ* and *ex situ* access and access to DSI. It should however be noted here that the majority of the stakeholders answering as provider countries selected the inclusion of DSI as the most favorable option. Nevertheless, three of them did not do so. While one of them gave a middle-low score, the other two gave inclusion of DSI the lowest score. According to one of the latter, the reason for this is that this stakeholder could see that it would be hampering research even in the stakeholder's own country.

Apart from two academic users, all of the user stakeholders found the inclusion of DSI the least favorable. One of them stated that it would not matter what is included in the scope as long as the regulatory requirements are not burdensome for whatever is covered in the ABS framework. One of the stakeholders who was against the inclusion of DSI suggested this to be handled in contracts rather than at the international level. This stakeholder argued that it is extremely challenging to define the limits of DSI in a unified manner. Another stakeholder from the collections argued that at the moment there is no way to track and trace DSI and, therefore, regulating it would be "a nightmare."

The responses of industrial users and collections varied regarding their choice of the most favorable option. A stakeholder from the collections opted for "*in situ* access only" as it would be easier for collections to provide genetic resources. One of the industrial users that chose "*in situ* and *ex situ* access" as the most favorable option stated that in the sector the stakeholder is familiar with (plant breeding), *ex situ* access would be much more favorable as that sector tends to access *ex situ* rather than *in situ*. Responses from industrial users in different sectors (e.g., pharma) as well as collections and academic users also demonstrated different tendencies toward *in situ* versus *ex situ* access.

Question 3 asked stakeholders to rank temporal scope options. The majority of the stakeholders opted for "access for utilization," which meant that they would prefer ABS obligations to be triggered at the moment of utilization of the genetic resource. "Access for sampling" took second place, whereas "access to a previously utilized genetic resource for new utilization" was the least favorable option. The preferences of the stakeholders in this question do not depend on the stakeholder group they belong in. For instance, where some stakeholders from the collections prefer the obligations to be triggered at the point of sampling (for it would bring legal certainty), others from the collections preferred that these obligations would be triggered at the point of utilization (as they believe that it may exclude most of the activities of collections). On the other hand, one of the academic users claimed that sampling in itself has no value and therefore should not be subject to ABS obligations.

Question 4 asked the preference of the stakeholders on what constitutes utilization. None of the options (research, development, R&D) had a significantly high preference rate as the choice of the stakeholders was scattered among all three options. Nonetheless, the option of utilization covering "R&D" got slightly higher votes than the others.

The vast majority of the stakeholders from collections opted for the ABS obligations to be triggered at the stage of research.

TABLE 2 | Stakeholders' preference on access.

	Material scope	Temporal scope	Utilization scope	Preconditions	Regulatory mechanisms	Granting authority	Standardization	Mandatory local partner	Facilitated access	Renegotiability
Providers	*In situ*, *ex situ*, and for DSI	Access for utilization	Development	Mandatory benefit-sharing agreement	Permit-based access	Centralized single institution	Case by case	Mandatory local partner	Facilitated access for non-commercial research	Renegotiable when user and intent change
Academic Users	*In situ* and *ex situ* access	Access for sampling and access for utilization	Development	No mandatory benefit-sharing agreement	Notification-based access	Centralized single institution	Case by case	No mandatory local partner	Facilitated access for non-commercial research	Renegotiable when user and intent change
Industrial Users	*In situ* and *ex situ* access	Access for utilization	Development	Mandatory benefit-sharing agreement	Notification-based access	Centralized single institution	Standardized and case by case[1]	No mandatory local partner	Facilitated access for non-commercial research	Renegotiable when user and intent change
Collections	*In situ* and *ex situ* access	Access for utilization	Research	No mandatory benefit-sharing agreement	Notification-based access	Centralized single institution	Standardized	No mandatory local partner	Facilitated access for non-commercial research	Renegotiable when user and intent change

[1]*There was no consensus among industrial users regarding this option.*

The majority of the industrial users however found "development" to be the most favorable trigger. Neither the provider countries nor the academic users opted for an option more than the others.

Question 5 asked the stakeholders whether there should be a mandatory benefit-sharing agreement concluded prior to access. A slight majority (11 stakeholders or 61%) opted for mandatory benefit-sharing agreement rather than a no benefit-sharing agreement or voluntary benefit-sharing agreement prior to access. While all of the stakeholders representing provider countries opted for the mandatory benefit-sharing, some of the stakeholders that represent users also opted for this option, stating that having an agreement prior to access would define user obligations and thus help secure legal certainty. Industrial users had a higher preference rate toward mandatory benefit-sharing agreement compared to academic users or collections.

Question 6 on the choice between requiring a notification for access against permit for access received varied responses. The majority of the stakeholders representing provider countries opted for requiring a permit for access, stating it as the only way to ensure benefit-sharing. Some of the provider representatives however argued that notification could be accepted for either local researchers or non-commercial researchers as a whole. Some stakeholders representing users stated that permit is the only way to ensure legal certainty and to be certain that their access will not be challenged in the future. Some of the users, on the other hand, stated that the lengthy permit processes create burden for research and the bureaucracy that comes with the permit system in some cases can jeopardize public health in times of disease outbreaks. One of the collection representatives stated that notification is enough for monitoring the utilization of genetic resources, and the administrative burden that comes along with permit processes results in either missing out opportunities for research funding or no research at all.

Question 7 asked the stakeholders whether they would prefer one centralized competent authority or several authorities based on either regional competence or the type of genetic resource. The vast majority of the stakeholders stated that they would prefer a centralized, single authority for various reasons. First, for it would allow better monitoring of genetic resources; second, that it would ensure a standardized evaluation process; third, that it would minimize disputes and communication problems between the authorities; and last, it would bring down transaction costs for both parties (the costs for users to evaluate applications and/or monitor genetic resources as well as costs for users to obtain access to genetic resources).

The preference on question 8, which asked stakeholders their thoughts on standardized or case-by-case conditions on access, had the highest score supporting case-by-case conditions by slight majority. Nevertheless, all of the stakeholders that opted for the case-by-case conditions stated that the ideal situation would be standardized terms that have the flexibility to be adapted to a specific case. Some of the stakeholders who chose standardized conditions also stated that they would prefer a model contract that can be tweaked to meet the needs of the case, type of genetic resource, and type of access.

Question 9 asked stakeholders to pick between an ABS framework requiring a local partner prior to access and an ABS framework that either does not require such a condition or encourages it on a voluntary basis. The majority of the stakeholders opted for the latter. Not all provider country representatives were supportive of mandatory local partners. One of the provider country stakeholders expressed the need for capacity development for nominating local partners who can successfully handle such a task. This stakeholder further argued that most providers do not have such capacity. One of the stakeholders representing industrial users stated that small companies would also not be able to handle such a mandatory requirement. A stakeholder from collections argued that local partners are only beneficial for long-term projects, and such long-term partnerships can help develop capacity in provider countries, yet would only be a burden in short-term efforts.

Question 10, which asked whether the stakeholders would prefer an ABS framework that provides facilitated access to non-commercial research as well as other types of research addressed under Article 8 of the Nagoya Protocol, the vast majority chose the provision of such access. A collections representative defined facilitated access as fewer, simpler conditions where the non-commercial user can agree to share useful information related to the genetic resource with the provider country. An academic user representative stated that facilitated access would entail clear information on when and with whom the provider will need renegotiation in case of commercial exploitation. One of the provider country representatives stated that such facilitated access should especially be given to foreign researchers as they require additional assistance in accessing genetic resources compared to their local colleagues.

Preferences on Benefit-Sharing

Questions 11–20 asked stakeholders how they perceive the impact and burden associated with several monetary and non-monetary benefits. These questions furthermore gathered insights from stakeholders regarding their preferences on the triggers and timing for benefit-sharing and the format and the mandatory nature of the benefits.

Non-monetary Benefits

Sharing Raw Data

The majority of the industrial users found sharing of raw data to be rather an ambiguous benefit-sharing option and a burdensome one. The majority furthermore exclaimed that the definition of raw data and what it entails are not clear. A way to encourage this is by giving the industry the choice of sharing it versus sharing other types of benefits.

Almost all of the interviewees from the collections were in favor of sharing raw data. The majority stated that generating data on genetic resources and making such data publicly available are highly beneficial for the collections and research dedicated to conserving biodiversity.

The vast majority of the interviewees from the provider countries stated that receiving raw data has a very positive impact. They however stated that there is some level of burden associated with it. Some of them stated that this burden comes from ensuring confidentiality to the data, and some of them stated that finding the right institution to share the data with to comprehend and make use of it is often challenging.

All of the academic users stated that sharing raw data would have a positive impact as academic researchers are also appreciative if the amount of publicly available raw data would increase. Some of them also argued that the term is rather ambiguous, and it should be standardized, or at least defined.

Sharing Research Results

The industrial users found sharing of research results to be a better option than sharing raw data. Yet, they stated that some burden is derived from inserting the research results into a usable format that is reader-friendly and is easy to disseminate.

The interviewees from the collections were all in favor of sharing research results as a type of benefit. They found it to have a very high positive impact also for their sector and stated that dissemination does not have much burden associated with it as it is one of their core activities.

Interviewees from provider countries found this option to be also highly beneficial for them, yet they stated that making sense of the results and being able to utilize them bear equal amounts of burden.

Academic users also expressed that sharing of research results is highly beneficial for them, and since it is their regular activity, such a benefit-sharing option would not be burdensome.

Capacity Building

The majority of the industrial users stated that this would have a relatively high positive impact, and the burden of executing such a benefit-sharing activity would not outweigh its impacts, whereas the majority of the interviewees from the collections stated that building capacity in provider countries has a highly positive impact both for the country and for the collections. They stated that capacity building helps establish more sustainable relationships with provider countries and also helps collections to ease into access procedures as mutual trust gets built.

This type of benefit-sharing is perceived by the majority of provider country participants to have a high positive impact. Some of the stakeholders argued that this would be the most important type of benefit-sharing as it would allow provider countries to valorize their own genetic resources, which they saw as the true meaning of the international ABS framework. However, they admitted that it would bear some limited amount of burden in ensuring that these activities would be received by the people who can utilize them.

While academic users stated that capacity building has a positive impact, they also argued that it has an equal amount of burden as the execution of capacity-building activities requires a relatively high amount of resources.

Technology Transfer

The interviewees representing the industrial users stated that this type of benefit-sharing has a high positive impact for them. Some perceived this to also have a positive impact for the provider country. Some argued that their scope of activities in conducting R&D with genetic resources results in a product or process that is a technology transfer activity in itself. Most of them also stated that technology transfer involves a limited to high amount of burden.

Likewise, the vast majority of the interviewees representing the collections found this to have a very positive impact. They added that compared to capacity building, technology transfer is a bit more burdensome.

Provider country participants stated that technology transfer is rather beneficial for them. However, learning and teaching how to make use of technology can sometimes be rather burdensome. Furthermore, the majority stated that not all technology they received was useful for them.

The majority of the academic users found technology transfer to have a lower amount of positive impacts than capacity building,

stating that often they are not allowed by their research partners to engage in such an activity.

Research Directed Toward Priority Needs of the Provider Country

The vast majority of the industrial users were in favor of this benefit-sharing option. One of them underlined that this would be the best approach for his sector as benefits would directly return to the people who need them. Yet, the majority agreed on it as a heavy burden because making sure the research precisely helps the provider country would require a considerable amount of resources.

While the majority of the interviewees representing collections stated that this would generate positive impact, some of them expressed concerns for this option, stating that the collections are extremely constrained at the type of research they can engage in, and therefore, they would not always be able to secure funding for such benefit-sharing.

The majority of interviewees representing provider countries stipulated that this is rather a minimally burdensome type of benefit-sharing with a high positive impact. One of the interviewees stated that provider countries regularly look into research gaps, and identifying the ones that could be filled by benefit-sharing would constitute limited burden.

The vast majority of academic users stated that this benefit-sharing option fits within their scope of activities, and therefore, they would be able to maximize the positive impacts of conducting such research.

Food and Livelihood Security Benefits

This option was perceived as beneficial by the majority of the industrial users. While acknowledging the positive impacts of food and livelihood security benefits, some interviewees stipulated that this type of benefit-sharing often does not have a connection with the utilization of genetic resource itself and that many industrial users engage in this type of benefit-sharing regardless of having accessed genetic resources from that country.

The responses from interviewees representing collections were rather varied. Some of them claimed that this type of benefit-sharing does not fit within their sector's scope of work, while others claimed that they have engaged in benefit-sharing activities that would be considered as food and livelihood security benefits. However, the majority argued that the burden of engaging in this option would outweigh the positive impacts.

Interviewees representing provider countries found this option to be the least impactful in terms of its positive effects for them, among other non-monetary benefits. One of the interviewees stated the reason for this as not being applicable to all of the regions or all of the provider countries. Nevertheless, the majority stated that the burden of receiving such a benefit would be minimal.

The interviewees representing academic users were not in favor of this option for their sector. While admitting it would still generate a limited amount of positive impact for them, it would also result in a heavy burden as this type of benefit-sharing is not something that they are used to see within their scope of activities.

Monetary Benefits

Joint Ventures

Almost all of the interviewees from industrial users stated that this would create a negative impact for their sector resulting also in very heavy burden. Some of the interviewees argued that, in some cases, a joint venture might work, but in any case, it should be a voluntary choice and not be imposed as a benefit-sharing clause.

The majority of the collections representatives stated that this option would constitute a very negative impact and even heavier burden. Some of them claimed that this type of benefit-sharing would only be relevant for applied research,[3] yet they stated that the burden of keeping that joint venture functional would outweigh any positive impact.

While the majority of the provider country representatives stated that there could be potential positive impacts deriving from a joint venture, they also stated that the cost of establishing and sustaining such an initiative would outweigh all potential benefits.

The majority of the academic users perceived this to have a positive impact. One of the interviewees claimed that this would give researchers a chance to work with local strains alongside local researchers that have knowledge on them.

Access Fee per Sample

Almost all of the interviewees from industrial users stated that such a benefit-sharing option would create negative impacts for their sector, arguing that it is not a realistic approach as most sectors work with thousands of genetic resources at the same time. Some claimed that this would be impossible for small and medium enterprises and start-ups as the cost of access would start impacting the R&D process from the first step of the value chain onward.

All of the interviewees representing collections stated that this option would result in very negative impact and very heavy burden, arguing that collections do not have the budget to pay such a fee for each access.

While the overall result points out to a positive impact for provider countries, some interviewees argued that this would not be a satisfactory approach as they stated that the price paid for a sample would not constitute benefit-sharing.

Even though the overall result is a positive impact for academic users, some remained skeptical about this option.

Up-Front Payments

For similar reasons to access fee *per* sample, the majority of industrial users found this option to have negative impacts and heavy burden for their sector. They argued that benefit-sharing at the beginning of the activity would be a huge drawback as it discourages R&D.

All of the interviewees representing collections stated that up-front payments would result in very negative impact and

[3] Upon receiving this response, these interviewees were asked to clarify the difference between basic/fundamental research and applied research. All of them agreed that there is no clear line between where one ends and the other begins. One of them stipulated that it is not possible to realistically talk about fundamental research today, since even for a single research funding, scientists need to talk about valorization, innovation, and end result.

very heavy burden. While agreeing with others, one of the interviewees stated that it might be interesting to share benefits up front if track and trace requirements would be removed by it and that the users would not have to worry about benefit-sharing at later stages.

The majority of provider country representatives perceived up-front payments to have a very positive impact in terms of being able to secure benefits from the starting point and being able to have less burden regarding enforcement and compliance.

The academic user interviewees did not have detailed opinions on this option. However, one remained skeptical, arguing that sharing monetary benefits from the get-go would negatively affect academic research.

License Fee

The responses from industrial user interviewees range from negative to very negative impacts as well as from heavy burden to very heavy burden. One of the interviewees argued that it is currently ambiguous what triggers sharing benefits as license fee. Another interviewee argued that license fees create a lot of administrative burden, which far outweigh positive impacts.

On the other hand, the vast majority of collections stated that this would not apply to them as collections do not engage in commercial activities with genetic resources. However, they claimed that if this would be applicable, it would create very negative impact and burden.

The responses from provider country representatives ranged from positive to very positive impacts, while burden was perceived to be limited. However, one of the interviewees opposed to it, arguing that imposing license fees would result in a lot of track and trace activities that create a heavy burden.

Although the majority of academic users perceived this benefit-sharing option to result in positive impacts and limited burden, they also refrained from clearly elaborating on the reason.

Royalties

The industrial user interviewees' responses did not create a consensus on the impact of royalties for their sector. One of the interviewees argued that royalties would be burdensome in terms of the administrative work it requires.

The collections mostly stated that this type of benefit-sharing does not have an impact nor a burden for their sector as they do not engage in commercial research.

The majority of provider countries were in favor of this option as they stated that it would create a very positive impact. Yet, most of them argued that the administrative burden of establishing a system to organize receiving this benefit type would constitute a heavy burden. One of the interviewees stipulated that royalties acknowledge the provider country's efforts to conserve biodiversity and create a good return on investment.

The majority of the academic user representatives did not have strong opinions against royalty payments. Some claimed that universities are prepared to execute such payment. Another one stated that collections may require a different type of benefit-sharing scheme, as this interviewee perceived collections' work as already a type of non-monetary benefit-sharing in terms of biodiversity conservation.

Salaries and Research Funding

Among all of the other monetary benefit options, interviewees representing industrial users were in favor of this option the most. One of the interviewees argued that this type of benefit-sharing would go to the people who really need them, and another argued that this is a very useful option for strengthening the sector's relationship with the provider country as they would be directly able to see the benefit that flows through the R&D on genetic resources.

Although the interviewees stated that the collections would have the least amount of burden in performing this benefit-sharing option, the majority still argued that collections do not have the capacity to provide such funding.

Provider countries did not favor this option as much as the latter two options. They stated that they would rather prefer funding for research, students, and capacity-building programs.

The majority of the academic users stated that they see this type of benefit-sharing (especially funding for PhD researchers) as one of their routine activities, and therefore, this would create minimal burden.

Trust Fund

The interviewees did not have a consensus on neither the impact nor the burden of this option. While some industrial users were indecisive about the effects it could have for their sector, some perceived it to be very beneficial.

Most of the interviewees from collections claimed that it would have no impact as they perceived that they would not be engaging in this type of benefit-sharing since they do not engage in commercial research. Some stated the benefit of a trust fund in terms of removing the burden of track and trace from both the user and the provider country.

Provider countries' responses ranged from positive to very positive. According to one of the interviewees, a trust fund would help better organize benefit-sharing and transparency of transactions while enabling the provider country to reduce the cost of compliance checks.

Likewise, the majority of academic users were in favor of this option in terms of its potential to also simplify access for researchers.

Mandatory Versus Voluntary

Mandatory benefit-sharing was the dominant option for industrial users. One interviewee held that the industry would prefer mandatory benefit-sharing to ensure legal certainty. Another interviewee argued that the ideal option would be making benefit-sharing mandatory yet allowing users to pick between monetary and non-monetary.

For collections, the answers were two-fold. Half of the collections claimed that to ensure legal certainty, mandatory benefit-sharing is key while the other half argued that many of the benefits arising from collections work cannot be predicted in advance and may be delivered over decades; a flexible system is more suited.

All of the interviewees representing provider countries preferred mandatory benefit-sharing. However, one stated that

it should be voluntary for local researchers. One interviewee claimed that his experience suggests voluntary benefit-sharing amounts to no benefit-sharing.

Only one of the academic users showed a tendency toward favoring mandatory benefit-sharing, arguing that provider countries will not be satisfied with a voluntary structure. The rest claimed that voluntary benefit-sharing would enable academic research to proceed.

Preset Versus Negotiated Conditions

For industrial users, the responses were two-fold. While the one half argued that small/medium enterprises (SMEs) would not be able to have resources to negotiate benefit-sharing agreements, the other half argued that everybody, including SMEs, has the means in its R&D budget to negotiate, and sometimes the flexibility provided by negotiation serves SMEs better. The former group furthermore argued that negotiating benefit-sharing each time an access happens bears too many transaction costs for both the user and the provider.

All of the interviewees representing collections were in favor of preset conditions as long as they would have some level of flexibility.

Provider countries' responses were not in unison. While some claimed that preset conditions would be very beneficial in terms of reducing transaction costs, some stated that not all cases would benefit from such an approach.

The majority of academic users also opted for preset conditions. Some stated that they should be flexible enough to be adapted to the case in hand and should not be hindering R&D.

Trigger for Benefit-Sharing

The majority of industrial users preferred sharing benefits some time after the user benefits from utilization of genetic resources (e.g., after the product has been in the market for a year).

While some interviewees stated that this should be access for collections as collections do not engage in commercialization activities, some claimed that it is better to have the trigger as late as possible.

The vast majority of provider countries were in favor of the trigger to be at the point of access, stating that this is the only way to secure benefits and arguing that track and trace for provider countries is almost impossible.

Most of the academic users preferred the trigger to be commercialization, stating that academic research should not be bound by benefit-sharing obligations if there is no applied research that follows after.

Perceptions on Compliance

Question 21 asked stakeholders their opinions on sanctions. The majority of the stakeholders preferred administrative fines for light breach, criminal sanctions for severe breach, while the least preferred option was criminal sanctions for all kinds of breach. Industrial users stated that they would prefer not to access genetic resources from countries that have criminal sanctions, especially for all kinds of breach. Academic users and collections stated the same regarding research activities. The majority of the provider countries emphasized the need to create proportionate sanctions.

CONCLUSION

This study identified common regulatory options implemented by provider countries when regulating their ABS matters. Regarding access, the author identified 25 options on access and 6 non-monetary and 7 monetary benefit-sharing options that are common to the provider countries' legislation subject to this study.

While describing the options, the research demonstrated some ambiguities regarding the definition and scope of some terms related to benefit-sharing. For instance, it was not possible to fully identify what constitutes sharing raw data, research results, or food and livelihood security benefits. Neither the international legal framework (CBD and the Nagoya Protocol) nor the COP Decisions prescribe what these benefit-sharing types exactly consist of. On the contrary, non-monetary benefit-sharing options, such as capacity building and technology transfer, are explained in detail at the international level. This comparative analysis furthermore noted that most of the ABS frameworks of the African countries subject to this study listed some benefit-sharing options within their legislation or annexed to the legal document without further describing them. It was noted that the majority of these options were identical to the options listed in COP Decision VI/24, also known as the Bonn Guidelines, which is the most detailed ABS guideline at the international level that got drafted before the Nagoya Protocol came into force. Although this seems to be a beneficial approach in terms of the national ABS frameworks' compatibility with the international ABS principles, the interview with stakeholders further demonstrated that neither the regulators nor the users exactly know what actions some of these benefit-sharing options entail.

Moreover, the comparative analysis demonstrates that, apart from some (such as Brazil, India, South Africa, and the Philippines), the provider countries' laws often do not expressly mention the trigger for benefit-sharing, meaning that the users would not be able to directly comprehend when they would need to share benefits. When this information is analyzed together with the data gathered from the provider country representatives during the interviews, we may think that this is perhaps because the majority of the provider countries opt for benefit-sharing at the point of access and that they presuppose the benefit-sharing will anyhow happen right after the PIC is granted and the mutually agreed terms (MAT) negotiated. This perception however needs to be tested in further detail.

The data related to access gathered during the stakeholder interviews lead to several conclusions. First, while the majority of the users do not favor the inclusion of DSI within the material scope, the majority of the provider countries do. This of course does not come as a surprise; however, an interesting point noted during the discussions is that even some of the provider country representatives admit that the inclusion would likely hamper the research, also for the local researchers in provider countries.

Regarding the activity that is included in the material scope, the participants agreed that the definition of utilization and the activities covered are yet to be clarified.

The data also demonstrate the ongoing lack of trust between users and provider countries. While provider countries want to subject access to a permit, users also want to be able to secure legal certainty from the get-go. In both cases, the stakeholders refer to previous biopiracy cases or allegations thereof as the underlying reason.

The responses from collections often demonstrate that they dissociate themselves from monetary benefit-sharing as there is a general perception among them that disentangles their scope of work with work that would require to share monetary benefits. They perceived that only commercial utilization would require monetary benefit-sharing.

It is also possible to see that both the users and provider countries still look for solutions to reduce transaction costs. The majority believes that multiple competent authorities in a country result in a lack of clarity and increase transaction costs, while most support facilitated access for basic research. However, some of the participants argued that the separation between basic and applied research is becoming increasingly complex. During the interviews, users in general repeatedly stated that complying with some ABS laws has proven to be especially difficult for non-commercial research and SMEs as the system is rather costly for them.

While some of the interviewees were not yet sure what to think of channelling benefits into a trust fund, the majority argued that such a benefit-sharing option would enable both the providers and the users to save on monitoring costs and that such a system could bring transparency into benefit-sharing. The stakeholders had a similar opinion regarding preset conditions for benefit-sharing. Although there is still no consensus on whether preset conditions would work, some stakeholders saw the benefit of them in terms of reducing transaction costs.

The results indicate a clash of opinions between provider countries and industrial users. Regarding benefit-sharing, where provider countries see a positive impact and minimal burden, industrial users often perceive negative impact and/or heavy burden. This is the case for sharing raw data and research results as well as paying access fee per sample and up-front payments. The clash also exists in providing salaries and research funding, where industrial users feel that it would create a very positive impact for them and for provider countries, yet the provider countries do not favor this option as much as the industrial users do. The trigger for benefit-sharing is another part where provider countries and the majority of the users disagreed. The providers stated that it would not be possible to retrieve benefits if they are not shared at the point of access, whereas the users in general stated that, in most cases, there is no benefit to share at the point of access as no utility is generated at that time.

Provider countries and industrial users do however feel the same way regarding some of the benefit-sharing options. For instance, both agree that capacity building is a very beneficial option with minimal burden. Likewise, they both agree with the fact that benefit-sharing should be mandatory. The majority of the industrial users expressed that the provider countries would not be satisfied with a voluntary benefit-sharing approach.

Apart from academic users, all of the stakeholders agreed that joint ventures, as a monetary benefit-sharing option, are heavily burdensome. It is perceived that the academic users perhaps do not associate a joint venture with establishing a joint corporate structure and carrying out the utilization of genetic resources under it (which is the way other stakeholders perceived joint ventures as such). For academic users, it seems that joint ventures indicate research collaborations with local institutions in the provider country.

While this study provides clarity to the perceptions of stakeholders on regulatory mechanisms commonly implemented by provider countries, further study is required both for finding a common ground between provider countries and industrial users and for a systematic analysis of each regulatory option's capacity to attain the international ABS goals. After all, a balanced ABS system would be associated with trust while dissociated with ambiguity and complexity.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

AUTHOR CONTRIBUTIONS

AS is the sole author of this manuscript.

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REFERENCES

Andean Community. (1996). Decision No. 391 Establishing the Common Regime on Access to Genetic Resources.

Anderson, P. V. (2003). *Technical communication – A reader-centered approach*. 5th ed. Boston: Heinle.

Australia. (2012a). Explanatory guide: model benefit-sharing agreement.

Australia. (2012b). Model access and benefit-sharing agreement between Australian Government and access party, Available at: http://www.environment.gov.au/system/files/pages/e3584028-d083-4aec-acdd-c0aa635a529f/files/commonwealth-and-access-party-model-benefit-sharing-agreement-2012.pdf.

Brazil. (2015). Law 13,123, dated May 20, 2015 To regulate paragraph 1, item II and paragraph 4 of Article 225 of the Federal Constitution; Article 1, Article 8(j), Article 10(c), Article 15, and Article 16, items 3 and 4 of the Convention on Biological Diversity, enacted by Decree no 2,519, dated March 16, 1998; to provide for access to genetic heritage, for protection and access to associated traditional knowledge, and for benefit-sharing for conservation and sustainable use of biodiversity; to revoke Provisional Act no. 2,186-16, dated August 23, 2001; and for other purposes.

CBD.int. (2019). "Capacity Building". https://www.cbd.int/cb/.

Cbd.int. (2011). *ABS Information Kit - English* [online] Available at: https://www.cbd.int/abs/information-kit-en/[Accessed 23 May 2019].

Costa Rica. (2003). Decreto N. 31514 del 3 de octubre de 2003 Normas Generales para el Acceso a los Elementos y Recursos Genéticos y Bioquímicos de la Biodiversidad.

Costa Rica. (1998). Ley de Biodiversidad 7788.

Crama, P., Reyck, B., and De, & Degraeve, Z. (2009). Milestone Payments or Royalties? Contract Design for R&D Licensing. *Operations Res.* 56 (6), 1539–1552. doi: 10.1287/opre.1080.0589

Dominican Republic. (2018). Regulation of access to genetic resources and distribution of benefits (ABS).

Ecuador. (2011). Reglamento Nacional al Régimen Común de Acceso a los Recursos Genéticos en aplicación a la Decisión N° 391 de la Comunidad Andina (Decreto Ejecutivo N° 905 de 3 de octubre de 2011).

Ethiopia. (2006). Proclamation No. 482/2006 access to genetic resources and community knowledge and community rights.

France. (2016). 3.1.LOI n° 2016-1087 du 8 août 2016 pour la reconquête de la biodiversité, de la nature et des paysages, les procédures d'accès et partage des avantages sur les ressources génétiques relevant de la souveraineté de l'Etat et les connaissances traditionnelles associées à ces ressources génétique.

France. (2017). France Ministère de la Transition écologique et solidaire Arrêté du 13 septembre 2017 fixant le contrat type de partage des avantages découlant de l'utilisation de ressources génétiques prélevées sur le territoire national, mentionné à l'article R. 412-20 du code de l'environnement.

Freeman, R. E., and McVea, J. (2001). A stakeholder approach to strategic management. Darden Business School Working Paper No. 01-02. Available at SSRN: https://ssrn.com/abstract=263511 or doi: 10.2139/ssrn.263511

India. (2014). Guidelines on access to biological resources and associated knowledge and benefits-sharing regulations.

Kenya. (2006). The environmental management and co-ordination act (No. 8 of 1999) environmental management and co- ordination (conservation of biological diversity and resources, access to genetic resources and benefit-sharing) regulations.

Kenya. (2013). An act of parliament to provide for the protection, conservation, sustainable use and management of wildlife in Kenya and for connected purposes [Act No. 47 of 2013, Act No. 19 of 2015, L.N. 105/2017.].

Laird, S. A., and Wynberg, R. P. (2018). A fact finding and scoping study on digital sequence information on genetic resources in the context of the convention on biological diversity and Nagoya Protocol. 3, 1–77. Available at: www.cbd.int/abs/dsi-gr/ahteg.shtmlpeerreview.

Malaysia. (2017). Access to biological resources and benefit-sharing bill.

Namibia. (2017). Access to biological and genetic resources and associated traditional knowledge bill.

Nagoya Protocol. (2011). Protocol on access to genetic resources and the fair and equitable sharing of benefits Arising from their utilization to the convention on biological diversity: text and annex. (Montréal: Secretariat of the Convention on Biological Diversity).

Norway. (2016). Regulations relating to the protection of traditional knowledge associated with genetic material Regulation | Date: 2016-11-25.

OECD (1993). Glossary of industrial organisation economics and competition law, compiled by R. S. Khemani, and D. M. Shapiro, commissioned by the directorate for financial, fiscal and enterprise affairs, OECD.

Philippines. (2005). Joint DENR·DA-PCSD·NCIP Administrative Order No. 1 Series of 2005 Guidelines for Bioprospecting Activities in the Philippines.

Republic of Korea. (2017). The Act on Access and Utilization of Genetic Resources and Sharing of Benefits. *Act. Genet. Resour*.

Republic of Korea. (2018). Ministry of Environment and Ministry of Foreign Affairs. A Guide to Act on Access to and Utilization of Genetic Resources and Benefit-Sharing in Republic of Korea.

Sirakaya, A. (2019). "Mutually supportive ABS system for users and providers: stakeholder perception on ABS goals," in press *Special Issue on Sustainability and Law*. (Wiley Journal on Sustainable Development).

Spain. (2007). Ley 42/2007, de 13 de diciembre, del Patrimonio Natural y de la Biodiversidad.

Spain, Ministry of Ecological Transition. (2019). Frequently asked questions regarding the application and authorization to access to Spanish genetic resources from wild taxa Available at: https://www.miteco.gob.es/en/biodiversidad/temas/recursos-geneticos/protocolo-de-nagoya/faq_autorizaciones.aspx. Accessed 16.05.2019.

Sittenfeld, A., and Gamez, R. (1993). *Biodiversity by INBio. Biodiversity prospecting: using genetic resources for sustainable development*. Washington: World Resources Institute, 69–98.

Shaw, D. M., Elger, B. S., and Colledge, F. (2014). What is a biobank? Differing definitions among biobank stakeholders. *Clin. Genet.* 85, 223–227. doi: 10.1111/cge.12268

South Africa. (2008). Regulations on Bio-prospecting, Access and Benefit-Sharing [Commencement of GN R138].

South Africa (2012). Department of environmental affairs, South Africa's bioprospecting, access and benefit-sharing regulatory framework: guidelines for providers, users and regulators.

Sustainabledevelopment. Un.Org. (2019). Capacity-Building: Sustainable development knowledge platform. *Sustainabledevelopment.Un.Org*. https://sustainabledevelopment.un.org/topics/capacity-building.

Swiderska, K. (2001). *Stakeholder Participation in Policy on Access to Genetic Resources, Traditional Knowledge and Benefit-Sharing, Case Studies and Recommendations*. International Institute for Environment and Development (IIED). https://pubs.iied.org/pdfs/9096IIED.pdf

Thailand. (2011). National committee on conservation and utilization of biological diversity regulation on the criteria and methods of the access and benefit-sharing of biological resources B.E. 2554.

Thailand, Office of natural resources, environmental policy and planning. (2014). *access and Benefit-Sharing*. Bangkok: Ministry of Natural Resources and Environment.

Uganda. (2005). Statutory instruments 2005 No. 30. The national environment (access to genetic resources and benefit-sharing) regulations.

Uganda. (2007). Guidelines for accessing genetic resources and benefit-sharing in Uganda.

UNEP. (2002). UNEP/CBD/COP/DEC/6/24 Bonn Guidelines on Access to genetic resources and fair and equitable sharing of the benefits arising out of their utilization.

UNEP. (2016a). CBD/COP/DEC/XIII/16 Digital sequence information on genetic resources.

UNEP. (2016b). CBD/NP/MOP/DEC/2/14 Digital sequence information on genetic resources.

United Nations Convention on Biological Diversity. (1992). 31ILM818, (entered into force Dec. 29, 1993).

Vietnam. (2017). Decree on the management of access to genetic resources and fair and equitable sharing of benefits arising from their utilisation.

World Intellectual Property Organization. (2004). Successful technology Licensing. *WIPO* (903), 1–52.

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POLICY AND PRACTICE REVIEWS
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The Cost of Postponement of Bt Rice Commercialization in China

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To maintain self-sufficiency in rice production and national food security, the Chinese government strongly supports research that aims at increasing the productivity of rice cultivation. Rice with genetic material from Bacillus thuringiensis (Bt rice) is transgenic rice that can reduce lepidopteran pest damage and the use of insecticides. It was developed in the 1990s and earned biosafety certificates in 2009. However, because of political reasons, its commercialization in China has been postponed, and, to date, Bt rice is not grown in China. We assess the opportunity cost of postponement of Bt rice commercialization in China between the years 2009 and 2019 and consider the external costs of pesticide use and potential technology spill-overs of Bt rice. We estimate the cost of postponement of Bt rice over the analyzed period to be 12 billion United States (US) dollars per year.

Keywords: Bt rice, cost of postponement, China, technology, trade

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INTRODUCTION

With only 6% of the world's fresh water and 7% of its arable land, China has to nurture nearly a fifth of the world's population (Wong and Chan, 2016). The arable land per capita in China decreased from 0.11 ha in 1990 to 0.09 ha in 2016, well below the world average of 0.19 ha per capita (World Bank, 2017b). Although rice is the predominant staple food in the country, the land allocated to its production decreased from 33.1 million ha in 1990 to 30.7 million ha in 2017 [National Bureau of Statistics of China (NBSC), 2018]. On the other hand, the amount of imported rice increased from 0.6 million metric tons in 2011 to 4.0 million tons in 2017, making China the biggest rice importer in the world (NBSC, 2018).

The United States (US) Census Bureau estimates that the Chinese population will reach 1.4 billion around 2026, which will further reduce the arable land per capita and increase the demand for rice. To maintain self-sufficiency in rice production and national food security, the Chinese government strongly supports research that aims to increase the productivity of rice cultivation. One of the priorities has, therefore, been the development of insect-resistant rice, such as rice with genetic material from *Bacillus thuringiensis* (Bt rice).

Bt rice is transgenic rice in which genes from the soil bacterium *Bacillus thuringiensis* have been transferred into the rice genome to reduce lepidopteran pest damage and the necessity of using insecticides (Huang et al., 2005). The yield of Bt rice can be up to 60% higher than conventional rice when no pesticides are used (Wang et al., 2010).

Chinese rice farmers apply more pesticides than farmers in most other countries (Huang et al., 2000). Huang et al. (2005) show, however, that Bt rice requires 80% less pesticide than conventional rice and reduces labor input (Rozelle et al., 2005). The simultaneous increase in production and reduction of input both contribute to the absolute increase of the total factor productivity of Bt rice, which is about 15% higher than conventional rice (Rozelle et al., 2005).

The adoption of Bt rice can also improve farmers' health due to lower exposure to pesticides (Huang et al., 2015). Bt rice is also compatible with biological control and soil health management, although it should be noted that, to the best of the authors' knowledge, no study examines its environmental effects at a larger scale or for a longer period (Cohen et al., 2008).

The cultivation of Bt rice in China requires special approval (Jin et al., 2019). The biosafety regulation system in China consists of three phases: field trials, environmental release trials, and preproduction trials. Before applying for field trials, Chinese scientists had spent 20 years investigating the thermal stability, digestibility, toxicity, and nutrient composition of Bt rice as well as the allergenicity of the Cry proteins it produces (Li et al., 2015). During various phases of the biosafety procedures, no food safety concern was raised. Bt rice is also found to be safe for aquatic ecosystems (e.g., Li et al., 2014) and has not shown any detrimental effects on non-target insect pests (Niu et al., 2017). It is expected to pose negligible risks to the non-target functional guilds in future large-scale Bt rice agroecosystems in China (Dang et al., 2017).

On October 22, 2009, China's Ministry of Agriculture (MoA)[1] issued biosafety certificates for two Bt rice lines (Cry1Ab/Ac Huahui No. 1 and Cry1Ab/Ac Bt Shanyou 63) (Chen et al., 2011). The issuance of the certificates indicates that the two lines are considered as safe as conventional rice, both to humans and the environment, and thus to be ready for commercialization. However, their official commercialization has been continuously postponed and is still pending. The biosafety certificates expired in 2014 but were renewed until the end of 2019.

The postponement of Bt rice commercialization is largely due to low public acceptance, like other genetically modified (GM) crops (e.g., Chen et al., 2014). Most Chinese business managers oppose food derived from GM crops because they fear lower profits (Deng et al., 2017). Although almost half of consumers know little about GM food, they believe it has adverse effects on human health and the environment (Qu et al., 2011). In addition, Chinese scientists do not show higher acceptance of GM food than non-scientists (Huang et al., 2017). Therefore, the government is hesitant to let China step forward as the first country to commercialize Bt rice.

More recently, however, the Chinese government has taken actions in policy support of the GM rice. In 2016, the "13th Five-Year Plan for Science and Technology Innovation" set an aim to push forward the commercialization of new domestic types of GM crops by 2020 (MoA, 2016).[2] In the same year, the MoA revealed a roadmap for commercialization of transgenic crops, starting with cash crops "not for food use" (e.g., cotton) followed by crops for feed and industrial use (e.g., maize and soybeans), then non-staple food crops (e.g., sugar beets), and finally staple food crops (e.g., rice) [MoA, 2016; US Department of Agriculture (USDA), 2016].

Xie et al., 2017 estimate that each 1-year postponement of commercializing insect-resistant GM maize in China leads to the opportunity costs in the range of 4–14 billion US dollars for the overall economy. Moreover, postponement of commercializing Bt rice has high opportunity costs because of its foregone potential economic and environmental benefits. In this respect, it is important to consider the foregone benefits of lower pesticide use associated with Bt rice as well as its technology spill-overs on the international rice price. These effects have been neglected so far in the relevant literature, and no economic analysis of the cost of postponement (CoP) of Bt rice commercialization in China is available. Our paper aims to bridge this gap in the literature.

To achieve our objective, we combine the Economic Surplus Model (ESM) with the Pesticide Environmental Accounting (PEA) Tool. The ESM has been widely used to assess the benefits and costs of technical changes in agriculture (Alston et al., 1998). A sample of previous uses of the ESM includes Wesseler et al. (2017), who estimated the foregone benefits of delayed approval of staple crops (bananas, cow peas, and maize) in Africa; Bayer et al. (2010), who quantified the regulatory costs of Bt rice, Bt eggplants, ringspot-virus-resistant papayas, and virus-resistant tomatoes in the Philippines; and Krishna and Qaim (2007), who investigated the welfare and distributional effects of the introduction of the Bt technology among eggplant farmers and consumers in India.

We estimate the external costs of individual chemicals in rice production using the PEA, which is considered an appropriate tool for estimating the benefits of technologies replacing pesticides (Leach and Mumford, 2008; Prannetvatakul et al., 2013).

We provide essential information for different groups of stakeholders, including domestic and foreign policymakers determining the commercialization of GM crops in general, particularly Bt rice, and for businesses interested in investing in new biotechnology.

MODEL FOR ASSESSMENT OF THE POLICY

The ESM (Alston et al., 1998) is a tool for ex-ante assessment of the consequences of current technology improvements. We use it

[1]The Ministry of Agriculture (MoA) transformed into the Ministry of Agriculture and Rural Affairs (MARA) in early 2018. The main difference after the transformation is the integration of sections of agricultural investment and management from different ministries, such as the Ministry of Finance and the Ministry of Land and Resources, into MARA. More details (in Chinese) are available at http://www.npc.gov.cn/npc/xinwen/2018-03/18/content_2050371.htm. The role of MARA in regulating genetically modified organisms (GMOs) has not changed significantly in comparison to the role of MoA.

[2]http://www.gov.cn/zhengce/content/2016-08/08/content_5098072.htm (in Chinese).

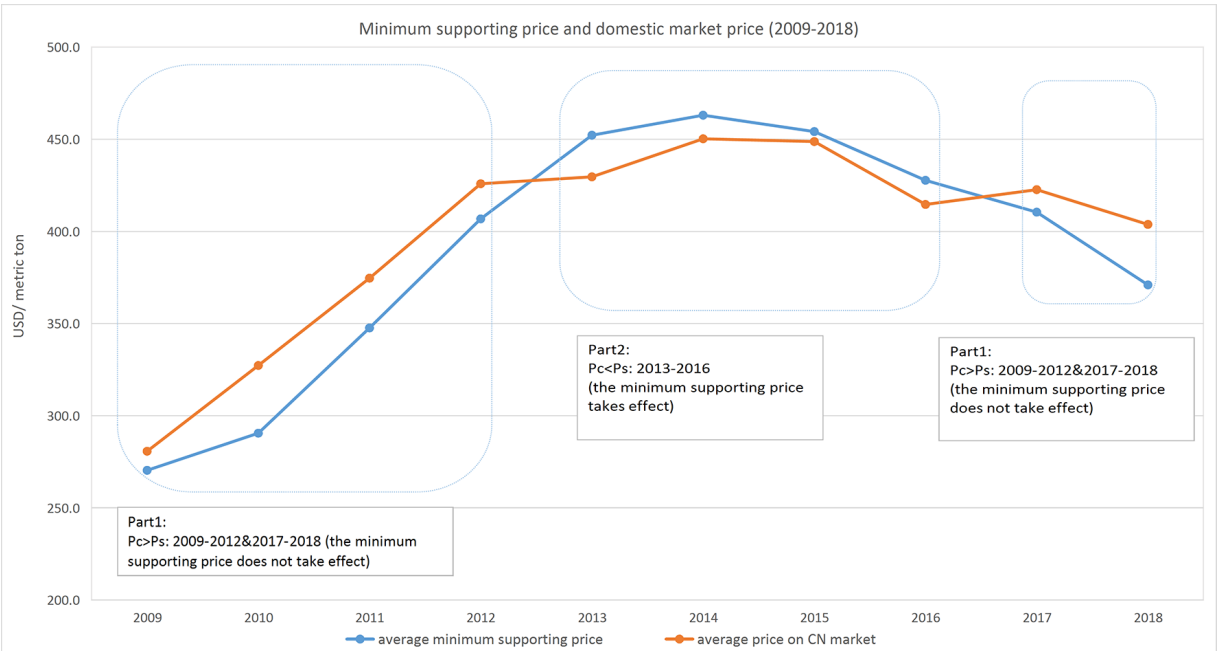

FIGURE 1| Minimum supporting price and domestic market price (2009-2018).

to calculate the welfare change between the counterfactual state of affairs had China commercialized Bt rice and the actual state of affairs due to the postponement of its commercialization. We model China as a large, open economy in rice trade. We set 2009 as the base year, since that is the year when Bt rice first received its biosafety certificate (MoA, 2009). Since then, Bt rice has been officially ready for commercialization.

The most important policy in China's price intervention program is the minimum supporting price. Since 2004, the minimum supporting price has been implemented for rice to maintain national food security and increase farmers' incomes.[3] Because of the increased total supply of rice, the Chinese government has to continuously buy rice from farmers to prevent the price from falling, even when massive stores of it already exist (Huang and Yang, 2017). **Figure 1** compares the minimum supporting price and domestic market price between 2009 and 2018.

Apart from the price intervention program, the Chinese government also implements a direct subsidy program for rice (and other grains). However, because the impact of agricultural subsidies on grain production has been shown to be negligible (Huang et al., 2011), we do not include this direct subsidy in the ESM.

We divide the 10-year period in **Figure 1** into two parts. Part 1 consists of the periods when the minimum price was lower than the domestic price (2009 to 2012 and 2017 to 2018), in which case the minimum price did not take effect. Part 2 consists of the period when the minimum price exceeded the domestic price (2013 to 2016).

[3]For wheat in 2006 and maize in 2008.

We assume that the rest of the world (ROW) agrees to trade in Bt rice but that it does not locally cultivate it.[4] The technology spill-over arises when the ROW follows China's adoption of Bt rice by also locally cultivating it. When the ROW cultivates Bt rice, the ROW supply curve shifts to the right, although typically not as much as the domestic Chinese supply does (Alston et al., 1998). The technology spill-over has an effect in China and the ROW by decreasing the world price. A lower world price benefits consumers in both China and the ROW, but producers in China lose due to the spill-over.

For the ESM to include the external costs of pesticide use that were introduced above, we assume there are no further research costs after 2009, since that was when the biosafety certificates of Bt rice were issued. Based on this assumption, the potential annual net benefits are the sum of foregone economic[5] and environmental benefits. This means that the potential annual net benefits (AB_t) after commercialization are equal to the sum of the change of annual welfare (ΔTS_t) and annual external costs of pesticides (TEC_{pt}):

[4]Recent developments support this assumption. For example, in January 2018, Bt rice was approved by the US Food and Drug Administration (FDA, 2018) and Environmental Protection Agency (EPA). This approval means that Bt rice can be consumed and imported to the United States but cannot be cultivated there.

[5]In the model, we use the annual total production of rice in the rice seasons (single or double-cropping rice) that have been taken into consideration. Therefore, different rice seasons in different regions in China will not influence the results. An important limitation of Bt rice is that it is developed to control lepidopteran pests but no other rice pests, such as plant hoppers. Herbicide is still needed for Bt rice to control weeds. Field trials of Bt rice revealed that pesticide is still needed (for non-lepidopteran pests) but that its amount could decrease significantly due to the resistance of Bt rice to lepidopteran pests.

$$AB_t = \Delta TS_t + TEC_{pt},$$

where t denotes the year ($t = 0$ corresponds to 2009).

We calculate the net present value of the potential annual benefits in 2009 and 2019 using the following equations:

$$NPV_{2009} = \sum_{t=0}^{\infty} (1+\mu)^{-t} AB_t$$

and

$$NPV_{2019} = \sum_{t=10}^{\infty} (1+\mu)^{-t} AB_t,$$

where μ denotes the discount rate of an infinite stream of annual benefits. The CoP is then given by the difference between NPV_{2009} and NPV_{2019}.

DATA SOURCES

The data come from both primary and secondary sources. The primary data are from the preproduction trial of Bt rice in China (R. Hu, private communication, 2017) and include the maximum adoption rate, yield, and input costs (Appendix 1). For the ESM, we calculate proportionate yield change and proportionate input cost change (per hectare) based on pesticide cost, labor cost, seed cost, fertilizer cost, and other costs. Because it takes time for farmers to adopt a new technology, we employ a logistic adoption function with a 55% ceiling.

All the secondary data come from official statistics and the literature (**Table 1**). The rice supply elasticity and the rice demand elasticity for China are based on Zhuang and Abbott (2007). The rice supply elasticity and rice demand elasticity for the ROW are based on Mohanty et al. (2017). The domestic price is from ChinaGrain (2018), and the minimum supporting price is from the Ministry of Agriculture and Rural Affairs (MARA). Because we do not have data on rice stocks, we assume that, in both China and the ROW, the annual consumption and production of rice are equal after adjusting for trade. The data on domestic production are available for the period from 2009 to 2016 from the official website of the NBSC. The rice production quantity for the ROW is available for the period from 2009 to 2016 from the Rice Yearbook of the USDA. For the remaining 3 years for which data are not yet available, we assume the quantities are the same as in 2016 (the same holds for prices after 2018).

Based on the data above, we calibrate the intercepts and slopes of supply curves and demand curves in China and the ROW. We use the calibrated parameters to simulate the new equilibrium price after commercializing Bt rice as well as new equilibrium quantities for the production and consumption in China and the ROW.

TABLE 1 | Parameterization and simulated results for the Economic Surplus Model in the period 2009-2019.

Raw parameters	unit	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*	Source
Initial domestic rice price	US dollar/ton	280.69	327.25	374.63	425.86	429.61	450.25	448.76	414.61	422.65	403.77	403.77	*ChinaGrain (2018)*
Initial CN rice consumption	million tons	194.67	195.53	201.08	206.33	205.41	205.41	211.32	210.15	210.15	210.15	210.15	*NBSC (2018)*
Initial CN rice production	million tons	195.1	195.76	201	204.24	203.61	203.61	208.23	207.08	207.08	207.08	207.08	*NBSC (2018)*
Initial ROW rice consumption	million tons	656.2	672.71	697.8	695.71	712.68	711.12	700.43	713.3	713.3	713.3	713.3	*USDA (2018)*
Initial ROW rice production	million tons	655.77	672.47	697.88	697.8	710.89	712.91	703.52	716.38	716.38	716.38	716.38	*USDA (2018)*
Supply shift relative to the initial equilibrium	unit free	0.02	0.11	0.2	0.2	0.19	0.18	0.17	0.16	0.15	0.14	0.13	*R. Hu, private comm. (2017)*
Simulated results													
Equilibrium rice price after adopting new technology	US dollar/ton	280.10	323.17	366.15	416.11	419.80	440.29	438.95	406.40	415.46	397.36	397.82	
CN rice consumption after adopting new technology	million tons	194.82	196.39	202.68	207.99	207.05	207.00	212.94	211.62	211.41	211.33	211.24	
CN rice production after adopting new technology	million tons	195.98	201.03	210.92	214.30	213.82	213.51	217.94	216.00	214.74	214.23	213.72	
ROW rice consumption after adopting new technology	million tons	656.60	675.14	702.39	700.34	715.61	715.70	704.89	713.03	716.83	716.60	716.36	
ROW rice production after adopting new technolog	million tons	655.44	670.50	694.15	694.03	708.84	709.19	699.89	713.03	713.50	713.69	713.88	

2019 Means that we use the value of the latest year to estimate the value in 2019.*

Since the biosafety certificates of Bt rice were already issued in 2009, we set the probability of success to 1, meaning that the new technology has already been successful in reality. For the same reason, we assume there are no further research costs after 2009. As for the discount rate, in our analysis, we apply both 3% and 5% rates to see the implications for the stream of benefits and costs from 2009 to 2019 (Bayer et al., 2010).

Tabashnik (2015) notes that some of the environmental, health, and economic benefits of Bt crops fade over time due to the evolution of pest resistance. We take this effect into account by considering a technology depreciation factor. For lack of data, we adopt the depreciation factor for Bt eggplant (Bayer, 2007). The factor equals one in the first 4 years. Starting in the fifth year, it decreases by five percentage points annually until it reaches 65%; from then, it remains constant at that level.

To calculate the external costs of pesticide use, we choose the three most commonly used rice pesticides in China (China Agrochemical Industry Network, 2012): Imidacloprid, Cartap hydrochloride, and Chlorantraniliprole. The percentage of the active ingredient of a certain pesticide and its application rates come from the product instructions. The base value of the external cost is calculated by Leach and Mumford (2008), and we use the US Inflation Calculator[6] to convert it to 2009 US dollars. We use the Environmental Impact Quotient (EIQ) calculator[7] to get the EIQ values for the three pesticides. We compare these values with the reference values for each category (Leach and Mumford, 2008) and determine whether a pesticide has a low, medium, or high level of toxicity. Based on the data from the World Bank (2018) and the NBSC (2009), we compare the ratio of China's share of employment in agriculture to the average share of agricultural employment in Germany, the United Kingdom (UK), and the US (weighted by gross domestic product [GDP]). We also compare the ratio of China's GDP per capita to the weighted average GDP per capita in Germany, the UK, and the US. Appendix 2 contains the details of the calculations.

RESULTS

Base Model

Using the PEA tool, we estimate the annual external costs of the uses of Chlorantraniliprole, Imidacloprid, and Cartap hydrochloride in China to be 1.8 million US dollars (0.06 dollars per hectare of agricultural land). (We calculated this amount using the equation and data presented in Appendix 2.) Considering that China banned a series of pesticides with a high level of toxicity in 2002,[8] the current pesticides used for rice are relatively environmentally friendly, which is also reflected in the annual external costs of pesticides.

[6]https://www.usinflationcalculator.com/
[7]https://nysipm.cornell.edu/eiq/calculator-field-use-eiq/
[8]http://www.chinapesticide.org.cn/fgzcwj/906.jhtml

Considering China as a large, open economy, the CoP of commercializing Bt rice from 2009 to 2019 is 104 billion US dollars under the 3% discount rate and 94 billion US dollars under 5% discount rate. We use the capital recovery factor (CRF) to calculate the annual CoP, which considers the time value of money and converts the CoP into a stream of equal payments from 2009 to 2019 at both the 3% and 5% discount rates. Under both discount rates, China loses approximately the same amount (12 billion US dollars) annually from 2009 to 2019 (**Table 2**).

Effect of the Technology Spill-Over

Different levels of technology spill-over in the ROW have implications for economic impacts on China (**Table 3**). We assume that the ROW's proportionate reduction in price due to the spill-over changes by 25%, 50%, 75%, and 100% compared to the base proportionate reduction in price. **Figure 2** shows the results.

With the increase in technology spill-over, the world rice price decreases. The lower world price benefits consumers in both China and the ROW. During the 10 years under study, China was a net importer in all years except for 2009 and 2010. **Figure 2** shows the effects of technology spill-over during this 10-year period. The total and annual CoP both increase when the level of technology spill-over increases. The percentage change in CoP is small, however. For example, at both 3% and 5% discount rates, the annual CoP increases by around 350 million US dollars when the technology spill-over rises from 0% to 100%: The relative change from the initial value is less than 3%.

Effects of the Maximum Adoption Rate and the Rate of Diffusion

We model the annual adoption rate (A_t) for Bt rice using the logistic function

$$At = \frac{\rho_{\max}}{1+e^{-\alpha-\beta t}},$$

where $\rho_{\max}$ denotes the maximum adoption rate, α represents a constant of integration, and the parameter β represents the rate of diffusion, which measures the rate at which adoption A_t increases with time t (Alston et al., 1998).

For the maximum adoption rate, no data are available, since Bt rice has not been approved for cultivation yet. The maximum adoption rate we use in the baseline is 55%,

TABLE 2 | Results of base model simulation (billion US dollars).

Discount rate (r)	NPV2009	NPV2019	CoP	CRF (unit free)	Annual CoP
3%	372	360	104	0.117	12.22
5%	224	212	94	0.130	12.15

Capital Recovery Factor (CRF) = [i(1+i)^n]/[(1+i)^n-1], where n = 2019-2009 = 10.

TABLE 3 | Sensitivity analysis of technology spillover.

	unit	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*
0% spillover												
Rice price	US dollar/ton	280.10	323.17	366.15	416.11	419.80	440.29	438.95	406.40	415.46	397.36	397.82
CN rice consumption	million tons	194.82	196.39	202.68	207.99	207.05	207.00	212.94	211.62	211.41	211.33	211.24
CN rice production	million tons	195.98	201.03	210.92	214.30	213.82	213.51	217.94	216.00	214.74	214.23	213.72
ROW rice consumption	million tons	656.60	675.14	702.39	700.34	715.61	715.70	704.89	717.41	716.83	716.60	716.36
ROW rice production	million tons	655.44	670.50	694.15	694.03	708.84	709.19	699.89	713.03	713.50	713.69	713.88
25% spillover												
Rice price	US dollar/ton	279.95	322.17	364.08	413.73	417.41	437.86	436.55	404.39	413.69	395.78	396.35
CN rice consumption	million tons	194.85	196.60	203.08	208.39	207.46	207.40	213.34	211.97	211.72	211.61	211.51
CN rice production	million tons	195.95	200.86	210.62	213.99	213.82	213.51	217.94	216.00	214.50	214.01	213.51
ROW rice consumption	million tons	656.70	675.74	703.51	701.48	716.76	716.81	705.98	718.42	717.70	717.41	717.11
ROW rice production	million tons	655.36	670.01	693.24	693.11	707.90	708.28	699.00	712.21	712.79	713.03	713.27
50% spillover												
Rice price	US dollar/ton	279.81	321.16	362.01	411.34	415.01	435.42	434.15	402.38	411.92	394.20	394.88
CN rice consumption	million tons	194.89	196.81	203.47	208.80	207.86	207.79	213.74	212.33	212.03	211.90	211.78
CN rice production	million tons	195.92	200.70	210.32	213.68	213.82	213.51	217.94	216.00	214.27	213.79	213.31
ROW rice consumption	million tons	656.80	676.34	704.64	702.61	717.91	717.93	707.07	719.42	718.57	718.22	717.87
ROW rice production	million tons	655.28	669.52	692.33	692.18	706.97	707.37	698.11	711.39	712.09	712.37	712.66
75% spillover												
Rice price	US dollar/ton	279.66	320.16	359.94	408.96	412.62	432.99	431.75	400.37	410.16	392.63	393.42
CN rice consumption	million tons	194.93	197.02	203.86	209.21	208.26	208.18	214.13	212.69	212.34	212.19	212.05
CN rice production	million tons	195.89	200.53	210.01	213.37	213.82	213.51	217.94	216.00	214.03	213.57	213.10
ROW rice consumption	million tons	656.90	676.94	705.76	703.74	719.06	719.05	708.16	720.43	719.43	719.03	718.62
ROW rice production	million tons	655.20	669.04	691.42	691.26	706.03	706.46	697.22	710.57	711.38	711.71	712.04
100% spillover												
Rice price	US dollar/ton	279.51	319.15	357.87	406.58	410.22	430.55	429.35	398.36	408.39	391.05	391.95
CN rice consumption	million tons	194.96	197.23	204.25	209.61	208.67	208.57	214.53	213.05	212.65	212.48	212.32
CN rice production	million tons	195.86	200.37	209.71	213.06	213.82	213.51	217.94	216.00	213.79	213.35	212.90
ROW rice consumption	million tons	657.00	677.55	706.88	704.87	720.22	720.17	709.25	721.44	720.30	719.84	719.38
ROW rice production	million tons	655.11	668.55	690.51	690.34	705.09	705.55	696.34	709.75	710.67	711.05	711.43

2019 means that we use the value of the latest year to estimate the value in 2019.*

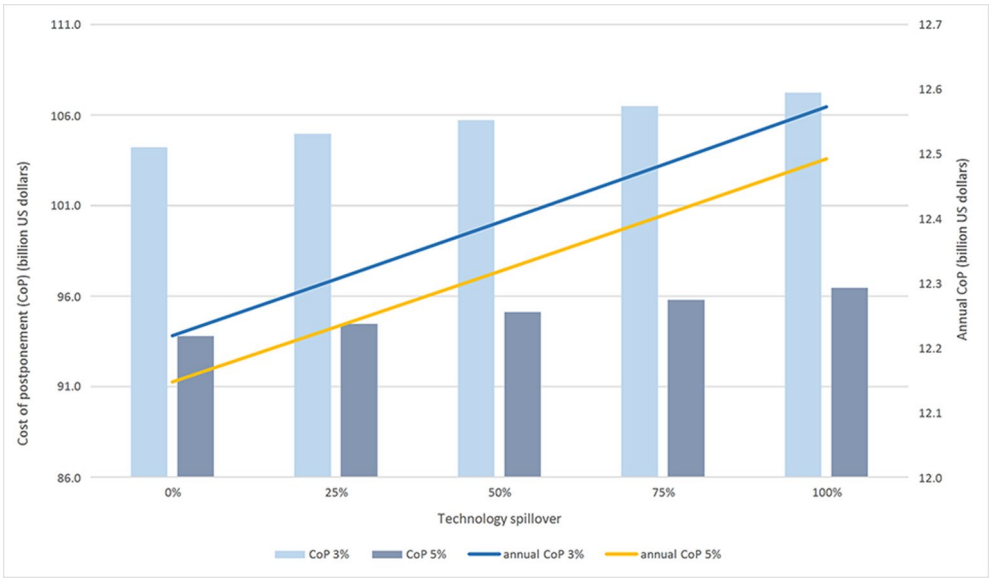

FIGURE 2 | Cost of postponement and technology spillover.

which corresponds to a preproduction trial (R. Hu, private communication, 2017). We assume the adoption rate for the first year is 5% ($A_1 = 0.05$). Since it took 3 years for the adoption rate to reach 55% in the preproduction trial in the period from 2002 to 2004, we set $A_3 = 0.54$ under the assumption that the adoption rate almost reached its maximum. Based on these assumptions, the calibrated parameters are $\alpha = -5.45$ and $\beta = 3.15$. In further sensitivity analyses (**Figure 3** and **Table 4**), we set the maximum adoption rate to 0.45, 0.55, 0.65, 0.75, 0.85, and 0.95 (and recalibrate the parameters α and β accordingly).

In another set of sensitivity analyses (**Figure 4** and **Table 5**), we examine the effect of the rate of diffusion (β) on CoP (holding ρ_{max} and α at their baseline levels) because the speed of adopting new technology is important when the cultivation area is large. We vary the parameter β between 1 and 6.

Both figures confirm that the economic benefits are larger the more farmers adopt Bt rice and the faster they adopt it. For example, when the maximum adoption rate increases by 10% (from 55% to 65%), the annual CoP increases by around 1.5 billion dollars. When the rate of diffusion gets larger, the speed of the increase in both CoP and annual CoP gets smaller. At both

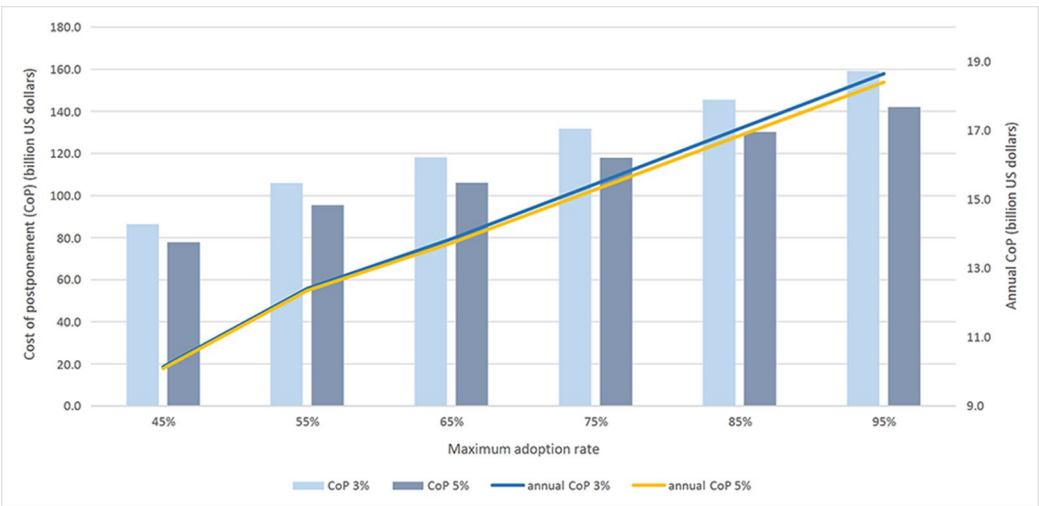

FIGURE 3 | Cost of postponement and maximum adoption rate.

TABLE 4 | Sensitivity analysis of maximum adoption rate.

	unit	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*
45% maximum adoption rate												
α	unit free	-5.01	-5.01	-5.01	-5.01	-5.01	-5.01	-5.01	-5.01	-5.01	-5.01	-5.01
β	unit free	2.93	2.93	2.93	2.93	2.93	2.93	2.93	2.93	2.93	2.93	2.93
Adoption rate	unit free	0.05	0.32	0.44	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45
Rice price	US dollar/ton	280.10	322.96	367.85	417.89	421.59	442.10	440.73	407.89	416.76	398.52	398.90
CN rice consumption	million tons	194.82	196.43	202.36	207.68	206.75	206.71	212.65	211.35	211.18	211.11	211.04
CN rice production	million tons	195.98	201.30	208.94	212.46	211.96	211.71	216.17	214.37	213.35	212.93	212.51
ROW rice consumption	million tons	656.60	675.27	701.47	699.50	714.75	714.86	704.07	716.66	716.19	716.00	715.80
ROW rice production	million tons	655.44	670.40	694.90	694.72	709.54	709.87	700.55	713.64	714.02	714.18	714.34
55% maximum adoption rate												
α	unit free	-5.45	-5.45	-5.45	-5.45	-5.45	-5.45	-5.45	-5.45	-5.45	-5.45	-5.45
β	unit free	3.15	3.15	3.15	3.15	3.15	3.15	3.15	3.15	3.15	3.15	3.15
Adoption rate	unit free	0.05	0.38	0.54	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55
Rice price	US dollar/ton	280.10	322.03	366.30	416.12	419.80	440.29	438.95	406.40	415.46	397.36	397.82
CN rice consumption	million tons	194.82	196.63	202.66	207.99	207.05	207.00	212.94	211.62	211.41	211.33	211.24
CN rice production	million tons	195.98	202.51	210.74	214.30	213.82	213.51	217.94	216.00	214.74	214.23	213.72
ROW rice consumption	million tons	656.60	675.83	702.31	700.34	715.61	715.70	704.89	717.41	716.83	716.60	716.36
ROW rice production	million tons	655.44	669.94	694.22	694.03	708.84	709.19	699.89	713.03	713.50	713.69	713.88
65% maximum adoption rate												
α	unit free	-4.58	-4.58	-4.58	-4.58	-4.58	-4.58	-4.58	-4.58	-4.58	-4.58	-4.58
β	unit free	2.09	2.09	2.09	2.09	2.09	2.09	2.09	2.09	2.09	2.09	2.09
Adoption rate	unit free	0.05	0.26	0.55	0.64	0.65	0.65	0.65	0.65	0.65	0.65	0.65
Rice price	US dollar/ton	280.10	323.68	366.15	414.59	418.05	438.48	437.17	404.91	414.15	396.19	396.73
CN rice consumption	million tons	194.82	196.28	202.68	208.25	207.35	207.29	213.24	211.88	211.64	211.54	211.44
CN rice production	million tons	195.98	200.37	210.92	215.87	215.64	215.31	219.71	217.62	216.13	215.53	214.93
ROW rice consumption	million tons	656.60	674.84	702.39	701.07	716.45	716.53	705.70	718.16	717.47	717.19	716.92
ROW rice production	million tons	655.44	670.75	694.15	693.44	708.15	708.51	699.23	712.42	712.98	713.20	713.43
75% maximum adoption rate												
α	unit free	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46
β	unit free	1.83	1.83	1.83	1.83	1.83	1.83	1.83	1.83	1.83	1.83	1.83
Adoption rate	unit free	0.05	0.23	0.55	0.71	0.74	0.75	0.75	0.75	0.75	0.75	0.75
Rice price	US dollar/ton	280.10	324.12	366.15	413.30	416.36	436.69	435.38	403.42	412.84	395.03	395.65
CN rice consumption	million tons	194.82	196.19	202.68	208.47	207.63	207.58	213.53	212.15	211.87	211.75	211.64
CN rice production	million tons	195.98	199.80	210.92	217.21	217.40	217.09	221.47	219.24	217.53	216.83	216.13
ROW rice consumption	million tons	656.60	674.57	702.39	701.68	717.26	717.35	706.50	718.90	718.11	717.79	717.47
ROW rice production	million tons	655.44	670.96	694.15	692.94	707.49	707.84	698.57	711.81	712.45	712.72	712.98
85% maximum adoption rate												
α	unit free	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46	-4.46
β	unit free	1.69	1.69	1.69	1.69	1.69	1.69	1.69	1.69	1.69	1.69	1.69
Adoption rate	unit free	0.05	0.21	0.55	0.77	0.83	0.85	0.85	0.85	0.85	0.85	0.85
Rice price	US dollar/ton	280.10	324.33	366.15	412.17	414.73	434.91	433.61	401.93	411.54	393.86	394.57
CN rice consumption	million tons	194.82	196.14	202.68	208.66	207.91	207.87	213.83	212.41	212.10	211.97	211.84
CN rice production	million tons	195.98	199.53	210.92	218.37	219.10	218.86	223.23	220.86	218.92	218.13	217.34
ROW rice consumption	million tons	656.60	674.45	702.39	702.22	718.05	718.17	707.31	719.65	718.76	718.39	718.03
ROW rice production	million tons	655.44	671.06	694.15	692.50	706.86	707.18	697.91	711.20	711.93	712.23	712.52

(*Continued*)

TABLE 4 | Continued

	unit	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*
95% maximum adoption rate												
α	unit free	-4.49	-4.49	-4.49	-4.49	-4.49	-4.49	-4.49	-4.49	-4.49	-4.49	-4.49
β	unit free	1.60	1.60	1.60	1.60	1.60	1.60	1.60	1.60	1.60	1.60	1.60
Adoption rate	unit free	0.05	0.21	0.55	0.83	0.92	0.94	0.95	0.95	0.95	0.95	0.95
Rice price	US dollar/ton	280.10	324.45	366.15	411.16	413.16	433.15	431.83	400.44	410.23	392.70	393.49
CN rice consumption	million tons	194.82	196.12	202.68	208.83	208.17	208.15	214.12	212.68	212.32	212.18	212.03
CN rice production	million tons	195.98	199.37	210.92	219.41	220.74	220.61	224.98	222.48	220.31	219.43	218.55
ROW rice consumption	million tons	656.60	674.38	702.39	702.69	718.81	718.98	708.12	720.40	719.40	718.99	718.59
ROW rice production	million tons	655.44	671.12	694.15	692.12	706.24	706.52	697.25	710.60	711.41	711.74	712.07

2019 means that we use the value of the latest year to estimate the value in 2019.*

3% and 5% discount rates, the annual C_OP doubles when the rate of diffusion changes from 1 to 6.

Actionable Recommendations

The results show that the continuous postponement of Bt rice introduction in China has come at a substantial economic cost that includes not only the direct economic losses of efficiency at higher prices of rice for consumers but also human health and environmental costs.

These costs have to be weighed against consumer concerns about Bt rice. Consumers, including those in China, tend to ignore the environmental benefits of crop production in their purchasing behavior. The introduction of Bt rice in combination with information about its environmental benefits, such as lower pesticide use and reduced greenhouse gas emission (Wesseler et al., 2011), may overcome some of the potential consumer resistance. Further, linking the introduction of Bt rice with a labelling policy might also increase consumer acceptance, as reported, for example, in the US (Kolodinsky and Lusk, 2018).

Our study suggests two main actionable policy recommendations. First, as further delays in the approval for Bt rice cultivation results in substantial costs, it should immediately be approved for cultivation. Second, for addressing potential consumer concerns, its introduction should be accompanied by a mandatory labelling of consumer products derived from Bt rice.

An additional policy recommendation is to link the approval of Bt rice cultivation with an information campaign about its environmental benefits. Further, Bt rice is just one example among several new crops developed using advances in plant breeding. The results presented for Bt rice carry over to many other crops, including Vitamin A-enriched rice (Wesseler and Zilberman, 2014), insect-resistant vegetables, such as eggplants and tomatoes (Groeneveld et al., 2011), and GMOs in general (Barrows et al., 2014). Studies show that delaying approval for the cultivation of these crops comes at substantial economic costs (see, for example, Zilberman et al., 2018). They not only directly benefit both farmers and consumers but also substantially benefit the environment, including, in some cases, substantial reductions in greenhouse gas emissions (Smyth et al., 2011). Policymakers in China should take these implications more explicitly into consideration when determining the approval of Bt rice and other crops developed using advanced plant-breeding technologies.

DISCUSSION

So far, no study has reported any adverse side effects of consuming food products derived from GM crops anywhere in the world (Paarlberg, 2009). Many scientific studies, to the contrary, present evidence that GM crops can be safely used in food and feed and are nutritionally equivalent to their non-GM counterparts (Snell et al., 2012; Bawa and Anilakumar, 2013). This also holds for the case of Bt rice (Li et al., 2014; Li et al., 2016).

TABLE 5 | Sensitivity analysis of rate of diffusion.

	unit	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*
β=1												
Rice price	US dollar/ton	397.84	327.02	373.95	424.00	425.79	443.93	440.66	407.00	415.66	397.43	397.84
CN rice consumption	million tons	211.24	195.58	201.21	206.64	206.05	206.42	212.66	211.51	211.37	211.31	211.24
CN rice production	million tons	213.69	196.06	201.79	206.15	207.59	209.89	216.24	215.35	214.53	214.15	213.69
ROW rice consumption	million tons	716.35	672.84	698.16	696.59	712.72	714.02	704.11	717.11	716.73	716.56	716.35
ROW rice production	million tons	713.89	672.36	697.58	697.08	711.18	710.55	700.52	713.27	713.58	713.72	713.89
β=2												
Rice price	US dollar/ton	280.49	325.83	369.25	416.81	419.91	440.31	438.95	406.40	415.46	397.36	397.82
CN rice consumption	million tons	194.72	195.83	202.10	207.87	207.04	207.00	212.94	211.62	211.41	211.33	211.24
CN rice production	million tons	195.40	197.60	207.30	213.58	213.71	213.50	217.94	215.99	214.74	214.23	213.72
ROW rice consumption	million tons	656.33	673.55	700.71	700.01	715.56	715.69	704.88	717.41	716.83	716.60	716.36
ROW rice production	million tons	655.66	671.78	695.51	694.30	708.88	709.19	699.89	713.03	713.50	713.69	713.88
β=3												
Rice price	US dollar/ton	280.18	322.51	366.39	416.12	419.80	440.29	438.95	406.40	415.46	397.36	397.82
CN rice consumption	million tons	194.80	196.53	202.64	207.99	207.05	207.00	212.94	211.62	211.41	211.33	211.24
CN rice production	million tons	195.87	201.89	210.65	214.29	213.82	213.51	217.94	216.00	214.74	214.23	213.72
ROW rice consumption	million tons	656.55	675.54	702.26	700.34	715.60	715.70	704.89	717.41	716.83	716.60	716.36
ROW rice production	million tons	655.48	670.18	694.26	694.03	708.84	709.19	699.89	713.03	713.50	713.69	713.88
β=4												
Rice price	US dollar/ton	279.46	320.32	366.16	416.11	419.80	440.29	438.95	406.40	415.46	397.36	397.82
CN rice consumption	million tons	194.98	196.99	202.68	207.99	207.05	207.00	212.94	211.62	211.41	211.33	211.24
CN rice production	million tons	196.93	204.72	210.91	214.30	213.82	213.51	217.94	216.00	214.74	214.23	213.72
ROW rice consumption	million tons	657.04	676.85	702.39	700.34	715.61	715.70	704.89	717.41	716.83	716.60	716.36
ROW rice production	million tons	655.08	669.11	694.16	694.03	708.84	709.19	699.89	713.03	713.50	713.69	713.88
β=5												
Rice price	US dollar/ton	278.16	319.86	366.15	416.11	419.80	440.29	438.95	406.40	415.46	397.36	397.82
CN rice consumption	million tons	195.29	197.08	202.68	207.99	207.05	207.00	212.94	211.62	211.41	211.33	211.24
CN rice production	million tons	198.85	205.32	210.92	214.30	213.82	213.51	217.94	216.00	214.74	214.23	213.72
ROW rice consumption	million tons	657.92	677.12	702.39	700.34	715.61	715.70	704.89	717.41	716.83	716.60	716.36
ROW rice production	million tons	654.37	668.89	694.15	694.03	708.84	709.19	699.89	713.03	713.50	713.69	713.88
β=6												
Rice price	US dollar/ton	276.57	319.79	366.15	416.11	419.80	440.29	438.95	406.40	415.46	397.36	397.82
CN rice consumption	million tons	195.68	197.10	202.68	207.99	207.05	207.00	212.94	211.62	211.41	211.33	211.24
CN rice production	million tons	201.20	205.40	210.92	214.30	213.82	213.51	217.94	216.00	214.74	214.23	213.72
ROW rice consumption	million tons	659.00	677.16	702.39	700.34	715.61	715.70	704.89	717.41	716.83	716.60	716.36
ROW rice production	million tons	653.49	668.86	694.15	694.03	708.84	709.19	699.89	713.03	713.50	713.69	713.88

2019 Means that we use the value of the latest year to estimate the value in 2019.*

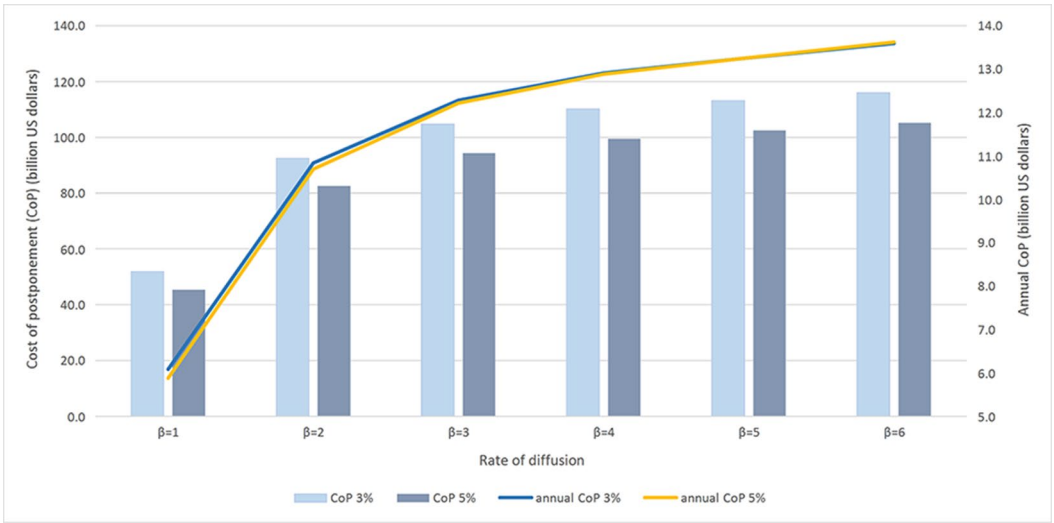

FIGURE 4 | Cost of postponement and rate of diffusion.

As a major producer, consumer, and trader of rice, China issued biosafety certificates for Bt rice in October 2009, which were renewed in December 2014, until the end of 2019; however, the commercialization of Bt rice in China has been continuously postponed and is still pending. We estimate the forgone benefits due to this postponement to be around 12 billion US dollars per year in the studied period (2009 to 2019).

This postponement is largely due to the low level of understanding and acceptance of GM crops in China (Li et al., 2016). Other challenges in commercializing Bt rice include resolving trade policy impediments and developing insect resistance management strategies (High et al., 2004; Liu et al., 2016). In January 2018, the US Food and Drug Administration and the US Environmental Protection Agency declared that Bt rice was not more dangerous than conventional rice and received legal clearance for import and consumption in the United States, indicating that Bt rice is likely to be approved in other countries in the future.

An important limitation of Bt rice is that it was developed to control lepidopteran pests but no other rice pests. Also, some lepidopteran pests are likely to increase their resistance to Bt rice after commercialization (Li et al., 2014); therefore, insect resistance management strategies are required before commercializing Bt rice. However, waiting for the identification of new genes to control non-lepidopteran pests or the development of new plant breeding technologies might result in sunk research and investment costs in Bt rice.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the manuscript/Supplementary Files.

AUTHOR CONTRIBUTIONS

YJ performed the calculations. DD and NH verified the analytical methods. JW helped shape the research and analysis.

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REFERENCES

Alston, J. M., Norton, G. W., and Pardey, P. G. (1998). *Science and scarcity*. New York, NY: CAB International.

Barrows, D., Sexton, S., and Zilberman, D. (2014). Agricultural biotechnology: the promise and prospects of genetically modified crops. *J. Econ. Perspect.* 28 (1), 99–120. doi: 10.1257/jep.28.1.99

Bawa, A. S., and Anilakumar, K. R. (2013). Genetically modified foods: safety, risks and public concerns—a review. *J. Food Sci. Technol.* 50 (6), 1035–1046. doi: 10.1007/s13197-012-0899-1

Bayer, J. C. (2007). Biotechnologies in the Philippines: the cost of regulation. A Master's thesis. Virginia Tech University. 1–63. Available at: https://theses.lib.vt.edu/theses/available/etd-06082007-105019/unrestricted/JBayerThesis.pdf (accessed 1 March 2018).

Bayer, J. C., Norton, G. W., and Falck-Zepeda, J. B. (2010). Cost of compliance with biotechnology regulation in the Philippines: implications for developing countries. *AgBioForum* 13 (1), 53–62.

China Agrochemical Industry Network. (2012). Introduction of rice pesticides. (in Chinese), available at: http://www.ccpia.com.cn/info.asp?classid=L010205&newsid=L206131605000566 (accessed 1 March 2018).

ChinaGrain. (2018). Domestic price of rice in China. (in Chinese), available at: http://datacenter.cngrain.com/KLineEnd.aspx?ID=18&Str=PD (accessed 1 March 2018).

Chen, M., Shelton, A., and Ye, G. Y. (2011). Insect-resistant genetically modified rice in China: from research to commercialization. *Annu. Rev. Entomol.* 56, 81–101. doi: 10.1146/annurev-ento-120709-144810

Chen, X., Yang, C., and Jia, H. (2014). Issues confronting GMO crops in China. *J. Huazhong Agric. Univ.* 33, 115–117.

Cohen, M. B., Chen, M., Bentur, J. S., Heong, K. L., and Ye, G. (2008). Bt rice in Asia: potential benefits, impact, and sustainability. *Prog. Biol. Control* 16, 223–248. doi: 10.1007/978-1-4020-8373-0_8

Dang, C., Lu, Z., Wang, L., Chang, X., Wang, F., Yao, H., et al. (2017). Does Vt rice pose risks to non-target arthropods? Results of a meta-analysis in China. *Plant Biotechnol. J.* 15, 1047–1053. doi: 10.1111/pbi.12698

Deng, H., Hu, R., Huang, J., Pray, C., Jin, Y., and Li, Z. (2017). Attitudes toward GM foods, biotechnology R&D investment and lobby activities among agribusiness firms in the food, feed, chemical and seed industries in China. *China Agric. Econ. Rev.* 9 (3), 385–396. doi: 10.1108/CAER-10-2016-0162

FDA (US Food and Drug Administration), 2018, available at: https://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/GEPlants/Submissions/ucm592625.pdf (accessed 1 March 2018).

Groeneveld, R., Ansink, E., van de Wiel, C., and Wesseler, J. (2011). Benefits and costs of biologically contained GM tomatoes and eggplants in Italy and Spain. *Sustainability* 3, 1265–1281. doi: 10.3390/su3081265

High, S. M., Cohen, M. B., Shu, Q., and Altosaar, I. (2004). Achieving successful deployment of Bt rice. *Trends Plant Sci.* 9 (6), 286–292. doi: 10.1016/S1360-1385(04)00099-8

Huang, J., Qiao, F., Zhang, L., and Rozelle, S. (2000). "*Economic and Environmental Program for Southeast Asia (EEPSEA)*," in *Farm pesticide, rice production, and human health* (Singapore: IDRC).

Huang, J., Hu, R., Rozelle, S., and Pray, C. (2005). Insect-resistant GM rice in farmers' fields: assessing productivity and health effects in China. *Science* 308, 688–690. doi: 10.1126/science.1108972

Huang, J., Wang, X., Zhi, H., Huang, Z., and Rozelle, S. (2011). Subsidies and distortions in China's agriculture: evidence from producer-level data. *Aust. J. Agric. Resour. Econ.* 55, 53–71. doi: 10.1111/j.1467-8489.2010.00527.x

Huang, J., Hu, R., Qiao, F., Yin, Y., Liu, H., and Huang, Z. (2015). Impact of insect-resistant GM rice on pesticide use and farmers' health in China. *Sci. China* 58 (5), 466–471. doi: 10.1007/s11427-014-4768-1

Huang. J., Wang, Z., and Dang, H. (2017). Impacts of and attitudes toward GM technology in China: challenges, policy and research implications. *China Agric. Econ. Rev.* 9 (3), 334–339. doi: 10.1108/CAER-07-2017-0131

Huang, J., and Yang, G. (2017). Understanding recent challenges and new food policy in China. *Glob. Food Sec.* 12, 119–126. doi: 10.1016/j.gfs.2016.10.002

Jin, Y., Drabik, D., Heerink, N., and Wesseler, J. (2019). Getting an imported GM crop approved in China. *Trends Biotechnol.* 37 (6), 566–569. doi: 10.1016/j.tibtech.2019.02.004

Kolodinsky, J., and Lusk, J. (2018). Mandatory labels can improve attitudes toward genetically engineered food. *Sci. Adv.* 6 (4), 1–5. doi: 10.1126/sciadv.aaq1413

Krishna, V. V., and Qaim, M. (2007). Potential impacts of Bt eggplant on economic surplus and farmers' health in India. *Agric. Econ.* 38, 167–180. doi: 10.1111/j.1574-0862.2008.00290.x

Leach, A. W., and Mumford, J. D. (2008). Pesticide environmental accounting: a method for assessing the external costs of individual pesticide applications. *Environ. Pollut.* 15 (1), 139–147. doi: 10.1016/j.envpol.2007.02.019

Leach, A. W., and Mumford, J. D. (2011). Pesticide environmental accounting: a decision-making tool estimating external costs of pesticides. *J. Consum. Prot. Food Saf.* 6 (1), 521–526. doi: 10.1007/s00003-011-0674-7

Li, B., Xu, Y., Han, C., Han, L., Hou, M., and Peng, Y. (2014). *Chilo suppressalis* and *Sesamia inferens* display different susceptibility responses to Cry1A insecticidal proteins. *Pest Manage. Sci.* 71 (10), 1433–1440. doi: 10.1002/ps.3948

Li, G., Wang, Y., Liu, B., and Zhang, G. (2014). Transgenic *Bacillus thuringiensis* (Bt) rice is safer to aquatic ecosystems than its non-transgenic counterpart. *PLoS One* 9 (8), 1–8. doi: 10.1371/journal.pone.0104270

Li, Y., Hallerman, E., Liu, Q., Wu, K., and Peng, Y. (2016). The development and status of Bt rice in China. *Plant Biotechnol. J.* 14 (3), 839–848. doi: 10.1111/pbi.12464

Liu, Q., Hallerman, E., Peng, Y., and Li, Y. (2016). Development of Bt rice and Bt maize in China and their efficacy in target pest control. *Int. J. Mol. Sci.* 17 (10), 1561–1576. doi: 10.3390/ijms17101561

MoA (Ministry of Agriculture of the People's Republic of China) (2009). List of biosafety certificates for agricultural products in 2009. (in Chinese), available at: http://www.moa.gov.cn/ztzl/zjyqwgz/spxx/(accessed 1 March 2018).

MoA (Ministry of Agriculture of the People's Republic of China) (2016). 12th five-year plan for economic and social development. (in Chinese), available at: http://jiuban.moa.gov.cn/zwllm/zcfg/flfg/201603/t20160307_5042893.htm (accessed 1 March 2018).

Mohanty, S., Chengappa, P. G., Hedge, M., Ladha, J. K., Baruah, S., Kannan, E., et al. (2017). *The future rice strategy for India*. Cambridge, USA: Academic Press.

NBSC (National Bureau of Statistics of China). (2009). *China statistical yearbook 2009*. Beijing: China Statistics Press. Available at: http://data.stats.gov.cn/ (accessed 1 March 2018).

NBSC (National Bureau of Statistics of China). (2018). *China statistical yearbook 2018*. Beijing: China Statistics Press. Available at: http://www.stats.gov.cn/tjsj/ndsj/2018/indexeh.htm.

Niu, L., Mannakkara, A., Qiu, L., Wang, X., Hua, H., Lei, C., et al. (2017). Transgenic Bt rice lines producing Cry 1Ac, Cry 2Aa or Cry 1Ca have no detrimental effects on brown planthopper and pond wolf spider. *Sci. Rep.* 7 (1), 1–7. doi: 10.1038/s41598-017-02207-z

Paarlberg, R. (2009). *Starved for science*. Cambridge, USA: Harvard University Press.

Prannetvatakul, S., Schreinemachers, P., Pananurak, P., and Tipraqsa, P. (2013). Pesticides, external costs and policy options for Thai agriculture. *Environ. Sci. Policy* 27, 103–113. doi: 10.1016/j.envsci.2012.10.019

Qu, Y., Chen, Y., Hou, Y., Huang, K., and Kang, D. (2011). Survey analysis of the cognition of GMO risk and safety among Chinese public. *J. China Agric. Univ.* 16, 1–10.

Rozelle, S., Huang, J., and Hu, R. (2005). Genetically modified rice in China: effect on farmers—in China and California. *Giannini Found. Agric. Econ.* 9 (1), 2–6.

Smyth, S., Gusta, M., Belcher, K., Phillips, P. W. B., and Castle, D. (2011). Environmental impacts from herbicide tolerant canola production in western Canada. *Agric. Syst.* 104, 4013–4410. doi: 10.1016/j.agsy.2011.01.004

Snell, C., Bernheim, A., Bergé, J. B., Kuntz, M., Pascal, G., Paris, A., et al. (2012). Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: a literature review. *Food Chem Toxicol.* 50, 1134–1148. doi: 10.1016/j.fct.2011.11.048

Tabashnik, B. E. (2015). ABCs of insect resistance to Bt. *PLoS Genet.* 11 (11), 1–5. doi: 10.1371/journal.pgen.1005646

USDA (US Department of Agriculture) (2016). China: agricultural biotechnology annual. available at: https://www.fas.usda.gov/data/china-agricultural-biotechnology-annual-2 (accessed 1 March 2018).

USDA (US Department of Agriculture) (2018). Rice yearbook. available at: https://www.ers.usda.gov/data-products/rice-yearbook/(accessed 1 March 2018).

Wang, Y., Zhang, G., Du, J., Liu, B., and Wang, M. (2010). Influence of transgenic hybrid rice expressing a fused gene derived from cry1Ab and cry1Ac on primary insect pests and rice yield. *Crop Protect.* 29, 128–133. doi: 10.1016/j.cropro.2009.10.004

Wesseler, J., Smart, R. D., Thomson, J., and Zilberman, D. (2017). Foregone benefits of important food crop improvements in Sub-Saharan Africa. *PloS One* 12 (7), 1–12. doi: 10.1371/journal.pone.0181353

Wesseler, J., and Zilberman, D. (2014). The economic power of the golden rice opposition. *Environ. Dev. Econ.* 19 (6), 724–742. doi: 10.1017/S1355770X1300065X

Wesseler, J., Scatasta, S., and Fall, E. H. (2011). "*Genetically modified food and global welfare*," in *Environmental benefits and costs of GM crops*, vol. 10 in Frontiers of economics and globalization series. Eds. Colin Carter, GianCarlo Moschini, and Ian Sheldon (Bingley, UK: Emerald Group Publishing), 173–199. doi: 10.1108/S1574-8715(2011)0000010012

Wong, A. Y., and Chan, A. W. (2016). Genetically modified foods in China and the United States: a primer of regulation and intellectual property protection. *Food Sci. Hum. Wellness* 5, 124–140. doi: 10.1016/j.fshw.2016.03.002

World Bank (2017a). Employment in agriculture. available at: https://data.worldbank.org/indicator/sL.AGr.empL.Zs (accessed 1 March 2018).

World Bank (2017b). Arable land (hectares per person). available at: https://data.worldbank.org/indicator/AG.LND.ARBL.HA.PC?order=wbapi_data_v (accessed 1 March 2018).

World Bank (2018). Gross domestic product 2018. available at: http://databank.worldbank.org/data/download/GDP.pdf (accessed 27 August 2019).

Xie, W., Ali, T., Cui, Q., and Huang, J. (2017). Economic impacts of commercializing insect-resistant GM maize in China. *China Agric. Econ. Rev.* 9 (3), 340–354. doi: 10.1108/CAER-06-2017-0126

Zhuang, R., and Abbott, P. (2007). Price elasticities of key agricultural commodities in China. *China Econ. Rev.* 18 (2), 155–169. doi: 10.1016/j.chieco.2006.02.006

Zilberman, D., Kaplan, S., and Wesseler, J. (2015). The loss from underutilizing GM technologies. *AgBioForum* 18 (3), 312–319.

Zilberman, D., Wesseler, J., Schmitz, A., and Gordon, B. (2018). Economics of Agricultural Biotechnology. Chapter 36 in Cramer, G. L., Paudel, K. P., and Schmitz, A. (eds.) The Routledge Handbook of Agricultural Economics, Routladge. 670-686.

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.

APPENDICES

APPENDIX 1 | Parametrization for the Economic Surplus Model.

Parameter	Description	Values and unit	Source
E(Y)	Proportionate yield change	0.045 (per hectare)	Personal communication
E(C)	Proportionate change in input cost	–21.4% (per hectare)	Personal communication
r	Discount rate (ESM)	discuss at 3% and 5%	Bayer et al. (2010)
ε_a	Domestic rice supply elasticity	0.273	Zhuang and Abbott (2007)
η_a	Domestic rice demand elasticity	–0.352	Zhuang and Abbott (2007)
ε_b	ROW rice supply elasticity	0.236	Mohanty et al. (2017)
η_b	ROW rice demand elasticity	–0.291	Mohanty et al. (2017)
$1\text{-}\delta$	Depreciation factor of technology	65%	Bayer (2007)
A	Maximum adoption rate	55%	Personal communication
q	Probability of adopting Bt rice	0.5	Assumption

The depreciation factor of technology starts in the 5th year and drops by five percentage points annually until 65%. ESM, economic surplus model; ROW, the rest of the world.

The annual total external costs of a pesticide p (TEC_p) can be calculated as

$$TEC_p = rate_p \frac{active_p}{100} \sum_{c=1}^{3} \left[EC_c F_c \left(F_{agemp} \big|_{c=1,2,3} \right) \right] F_{gdppc},$$

where $rate_p$ denotes the application rate of a pesticide p in kilograms of formulated product per hectare and $active_p$ denotes the percentage of active ingredient in the formulated product (Prannetvatakul et al., 2013).

The PEA uses the Environmental Impact Quotient (EIQ) calculator to adjust the base values of economic costs to differences between relative toxicities of pesticides. There are eight events within three large categories in the EIQ with 472 active pesticide compounds in total: (*i*) farm workers,[9] (*ii*) consumers,[10] and (*iii*) the environment.[11] In the study, we aggregate eight events into three categories and convert EIQ values to external costs for the three categories with subscript c = 1, 2, or 3 representing the categories (*i*), (*ii*), or (*iii*), respectively. The PEA tool converts EIQ values for the three categories to external costs by multiplying the external cost base values with a factor F_c that has three levels: 0.5 if the pesticide has a relatively low toxicity level; 1.0 if it has a medium toxicity level; and 1.5 if it has a relatively high toxicity level. Leach and Mumford (2008) define the ranges of toxicity level for each category.

EC_c is the base value of external costs calculated by Leach and Mumford (2008) converted to 2009 US dollars. The parameter F_{agemp} denotes the ratio of China's share of employment in agriculture to the average share of agricultural employment in the Unites States (US), the United Kingdom (UK), and Germany weighted by the gross domestic product (GDP). F_{agemp} takes into consideration that, in China, more people are engaged in agriculture than in the other three countries, thus having more direct contact with pesticides.

The parameter F_{gdppc} denotes the ratio of China's GDP per capita to the average GDP per capita in the US, the UK, and Germany, weighted by the GDPs of those countries. F_{gdppc} considers that, due to lower labor costs in China, lower costs of monitoring and cleaning up lead to lower external costs (Prannetvatakul et al., 2013).

[9]The effects on applicators and pickers.
[10]The effects of pesticide residues on groundwater leaching and food consumption.
[11]The effects on aquatic life, bees, birds, and beneficial insects.

APPENDIX 2 | The Parametrization of the Pesticide Environmental Accounting (PEA) Tool.

	$rate_p$	$active_p$	EC_1	EC_2	EC_3	F_1	F_2	F_3	Fagemp (c = 1,2,3)			Fgdppc
Chlorantraniliprole	0.001	0.2	1.8	6.09	2.76	0.5	0.5	0.5	20.243	1	1	0.085
Imidacloprid	0.041	0.7	1.8	6.09	2.76	0.5	0.5	0.5	20.243	1	1	0.085
Cartap hydrochloride	0.003	0.98	1.8	6.09	2.76	0.5	0.5	0.5	20.243	1	1	0.085
Source	Personal calculation based on data from www.taobao.com		Cornell EIQ calculator: https://nysipm.cornell.edu/eiq/calculator-field-use-eiq			Leach and Mumford (2008)			Personal calculation based on data from World Bank (2018) and NBSC (2009)			

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Challenges of Justice in the Context of Plant Genetic Resources

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In this article, I discuss access and benefit-sharing (ABS) for plant genetic resources from an ethical perspective. This leads to the question of what types of justice actually play a role when more equity and fairness is demanded for plant genetic resources. Five dimensions of justice will be distinguished: classical distributive justice, which deals with a fair distribution of goods; commutative justice, which concerns a fair exchange of "give-and-receive"; justice as recognition, which relates to treating all involved parties with the same respect; reparative justice, which pertains to fair amendments for wrongful actions in the past; and procedural justice, which is concerned with just decision processes. Drawing on the discussion of ethical problems with biopiracy, the distribution of environmental burdens, and plant genetic resources in agriculture, I will illustrate that the use of genetic resources poses challenges across all five dimensions of justice. Because the combination of justice challenges is specific for each case of resource use, I will argue that it is important that users of genetic resources are aware of the complexity of justice problems to ensure fair and equitable ABS negotiations.

Keywords: access and benefit-sharing, commutative justice, Convention on Biological Diversity, distributive justice, environmental justice, genetic resources

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"Justice" is a paramount ideal underlying the debates on how to regulate and use plant genetic resources. We discuss questions such as *Who has rights to access and use these resources? How should benefits be shared? How should the use of genetic resources be regulated? Who should be involved in discussing these questions?* All of these are questions concerning justice. They are asked and discussed with the aim of finding answers that take into account what is due to all those who have a stake in genetic resources. I have written this overview article from an understanding of justice in analytic philosophy.[1] Although there is wide agreement that justice is important, there may be different views on what it means to safeguard justice in the development of policy as well as in specific access and benefit sharing negotiations. One reason for such disagreement is that justice is a concept with different dimensions. I will distinguish between five such dimensions, which all play a role in dealing with genetic resources. The aim of this analysis is to contribute to the understanding of first, why the use of genetic resources generates so much attention and controversy, and second, what needs to be considered in regulating and handling them justly. By discussing these issues, I am addressing not only philosophers but also an interdisciplinary readership, hoping that the article provides an occasion for them to take a step back from the everyday occupation with genetic resources and to reflect on the ethical implications associated with their use. Ideally, this will contribute toward bringing more justice reflections into

[1] Even though justice in this sense requires considering other worldviews as part of doing justice to other communities, it cannot be denied that the approach itself is driven by a particular Western tradition of thought. It would be beyond the scope of this article to consider different cultural approaches to justice, but this work may serve as a starting point for a wider intercultural comparison. Moreover, I would like to clarify that this is not a work in legal theory, which interprets justice within a legal framework but rather in moral philosophy, reflecting on how the legal framework should be constructed in order to be able to respond and solve ethical challenges of justice.

the drafting or implementing of regulatory schemes. Moreover, these reflections may facilitate specific access and benefit-sharing (ABS) negotiations, which may be complicated by the fact that the different parties are prioritizing different dimensions of justice possibly without awareness of this source of disagreement.

After a brief introduction of the conception of justice underlying this article, each of the five dimensions of justice will be presented separately. For this purpose, I will start with a general introduction of the particularities of the respective justice dimension followed by a discussion of the role that it plays in the context of genetic resources. In doing so, I will draw on my own previous research and connect it to the philosophical work of other authors, for instance, Bram de Jonge and Doris Schroeder. Moreover, I will connect the literature on justice for genetic resources with parallel discourses on environmental justice or restorative justice. The presentation of the five dimensions of justice will be followed by the discussion of three practical justice challenges to illustrate how the justice dimensions meet: first, biopiracy; second, the distribution of environmental burdens; and third, plant genetic resources in agriculture. The article will close with two practical conclusions for a fair and equitable use of plant genetic resources.

FIVE DIMENSIONS OF JUSTICE IN DEALING WITH GENETIC RESOURCES

The three most influential international treaties that introduced ABS for genetic resources are the Convention on Biological Diversity (CBD),[2] the Nagoya Protocol (NP),[3] and the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA).[4] These treaties have the explicit objective to ensure "fair and equitable sharing of benefits" from genetic resources. In spite of the prominence of the clause "fair and equitable," for instance, in the full title of the Nagoya Protocol, and notwithstanding the long tradition that this clause has in investment treaties (Dolzer, 2005), its meaning remains undefined and vague (De Jonge, 2011; Vermeylen and Walker, 2011; Morgera, 2015). It is evident, however, that in one way or another fair and equitable benefit-sharing aims at introducing justice into the regulation and use of genetic resources. In that sense, Bram de Jonge discusses the question, *What is fair and equitable benefit-sharing?* by analyzing different principles of justice (De Jonge, 2011), and Morton Walloe Tvedt and Tomme Young also raise mainly justice topics in their analysis of the meaning of "fair and equitable" in ABS (Tvedt and Young, 2007: pp. 83–91).

For the purpose of this article, I assume that justice is a morally weighty demand, and I start from a very basic and general meaning of "justice" going back to the Roman law, where it was defined in the Institutes of Justinian as "the set and constant purpose which gives to every man his due" (Justinian, 1913: Book I, Title I). In a modern view, influenced by Enlightenment philosophy, this means that justice is based on the acknowledgment that all human beings have equal moral status and basic moral rights. I will distinguish between five different dimensions of justice: distributive justice, which deals with a fair distribution; commutative justice, which concerns a fair exchange of give-and-receive; justice as recognition, which relates to treating all involved parties with the same respect; reparative justice, which pertains to fair amendments for wrongful actions in the past; and procedural justice, which is concerned with just decision processes (For an overview, see **Table 1**). Each of these justice dimensions takes up other aspects of what it means to give everybody their due. The aim of the following introduction of the five dimensions of justice is not to suggest what a just ABS system for genetic resources would look like. Instead, I attempt to contribute to a better understanding of the challenges at hand and the reasons why there is controversy surrounding how to solve them.[5]

Let me start now with the presentation of the five dimensions of justice, which refer to different aspects of what we owe to others.

DISTRIBUTIVE JUSTICE

Distributive justice is concerned with fair distribution of, for instance, material goods, such as natural resources. A large body of literature is dedicated to the question of who has rights to own, control, or benefit from natural resources (e.g., Nine, 2012; Armstrong, 2017). Key questions in that discourse are to what extent nation states have exclusive rights to benefits from natural resources that are found on state territory, and whether or how all people around the globe should be able to benefit at least partially from those resources. Besides natural resources, the distribution of non-material goods, such as power or opportunities, has also received wide attention in political philosophy (Rawls, 1971; Dworkin, 2000). Although distributive justice can be based on the idea that a just distribution provides an equal share of the distributed good to each party, there are also alternative views. John Rawls, for instance, famously suggested a "difference principle" which is based on a maximin criterion, meaning that unequal distribution of income or wealth can be just if this distribution still leads to advantages for the worst-off party compared with the available alternatives (Rawls, 1971).

In addition to the importance of a fair distribution of *goods*, more recently the demand for distributive justice has also

[2] The text of the Convention on Biological Diversity is available at: https://www.cbd.int/convention/text/ (accessed May 2019).

[3] The text of The Nagoya Protocol is available at: https://www.cbd.int/abs/ (accessed May 2019).

[4] The text of the International Treaty on Plant Genetic Resources for Food and Agriculture is available at: http://www.fao.org/plant-treaty/overview/texts-treaty/en/ (accessed May 2019).

[5] The five dimensions of justice should be understood as heuristic groups, which serve the aim of facilitating the analysis of justice questions that arise. I am not aiming at developing a theory of justice, I do thus not rank the dimensions of justice; none of them is treated as having general priority over the other. Moreover, I do not take any position as to whether one justice dimension is generally primary to another one. Therefore, I do, for instance, not argue in favour of or against Axel Honneth's position according to which unjust distribution is a result of misrecognition (Fraser and Honneth, 2003). I acknowledge, however, that the different dimensions of justice can overlap. An unjust situation can concern more than one justice dimension. In the context of environmental justice, Gordon Walker, for example, highlighted that different dimensions of justice are often closely linked, procedural injustice can be an explanation for distributive injustice (Walker, 2012: p.47); then again, unjust distribution of power and money or misrecognition of certain communities can be a cause for unjust procedures.

TABLE 1 | Comparing the different justice dimensions when justice in general means that everybody gets his or her due.

Justice dimension	
Distributive justice	To give everybody their due shares in benefits and costs.
Commutative justice	To give everybody the due compensation in exchange for a good or service that was provided.
Justice as recognition	To give everybody their due respect.
Reparative justice	To give due redress to those who suffered injustice and possibly due punishment to those who committed it.
Procedural justice*	To give everybody their due voice and participation in decision making processes.

**Procedural justice is defined in the narrow sense used in the environmental justice discourse.*

been expressed regarding global and local *bads*. Distributive justice in this sense is one central pillar of the concept of "environmental justice" that goes back to a grassroots movement in the 1990s in the United States. The movement pointed to the existing environmental injustice when environmental risks and burdens, such as waste dumpsites, toxic emissions or other contaminations, are unequally distributed. Some communities endure more environmental burdens than others, and often, it is previously disadvantaged, marginalized, or impoverished groups that, in addition to these social injustices, also suffer environmental injustice (Bullard, 1993; Schlossberg, 2007; Walker, 2012).

Distributive Justice for Genetic Resources

Distributive justice is one of the most widely discussed justice dimensions in the literature on genetic resources (e.g. De Jonge and Korthals, 2006; Korthals and De Jonge, 2009; Schroeder and Pogge, 2009; Schroeder and Pisupati, 2010; Vermeylen and Walker, 2011; Deplazes-Zemp, 2019). The term "genetic resources" suggests that they are a type of natural resource, a view also supported by the current regulatory framework in which genetic resources are placed under state sovereignty over natural resources. The understanding of genetic resources as a type of natural resource directly links this discussion to the literature on resource rights (Deplazes-Zemp, 2019). However, to treat genetic resources analogously to other natural resources may be problematic because genetic resources are a very particular type of natural resource. They can be described as atypical with respect to first, their non-tangible nature; second, the close connection between natural and cultural formation; as well as third, their connection to biodiversity and its vulnerability (Deplazes-Zemp, 2018b). These three features of genetic resources are relevant when it comes to distributive justice (Deplazes-Zemp, 2019), therefore, I will explain each of them in some more detail. It has been highlighted that genetic resources are non-tangible and that they carry information (Vogel, 1994; Millum, 2010; De Jonge, 2011; Tvedt and Schei, 2013; Ruiz Muller, 2015; Deplazes-Zemp, 2018b). I thus speak of the "informational" nature of these resources and suggest that this particular feature can best be illustrated by contrasting genetic resources with other biological resources such as timber or fish. While benefits from the latter are material and used as food or building material, it is the information in genetic resources that is of value among other things because it can lead to the generation of new material outside the provider country. According to such an interpretation of genetic resources it is thus the information that is exported from the country of origin and used and propagated, for instance in breeding processes or in biological or chemical procedures (Vogel, 1994; De Jonge, 2011; Ruiz Muller, 2015; Deplazes-Zemp, 2018b).[6] The informational nature implies that territorial claims of countries of origin are more difficult to legitimize for genetic resources than for material natural resources. While in the case of material resources a constant supply from the country of origin is required for their use, in the case of genetic resources, only a one-time extraction of a small material sample is needed. Therefore, the territorial connection of the latter type of resource is weaker.

Although the question of how to share *material* or *financial* benefits from genetic resources is central to the debate, the Annex of the NP also lists a variety of potential *non-monetary* benefits from genetic resources that could be shared and that could be understood as a distribution of opportunities. The list includes benefits such as research collaboration, admittance to databases, access to scientific information, capacity-building and training.[7] In addition, Bram de Jonge and Michiel Korthals suggest that "upstream benefit-sharing" should also be taken into account for distributive justice; by this, they mean opportunities and power to influence research and development agendas in the context of genetic resources (De Jonge and Korthals, 2006; Korthals and De Jonge, 2009). The authors suggest that this distributive aspect should be considered in decision making procedures for different uses of genetic resources, which directly relates to what I will discuss later in the sections on justice as recognition and procedural justice.

Finally, the third atypical feature of genetic resources is that they are related to biodiversity through the diversity of species that actually or potentially carry genetic resources. Biodiversity could also be the source of evolution of novel genetic resources in the future, and it is the condition for intact ecosystems in which current genetic resources prosper. This connection implies that genetic resources are vulnerable to decimation and extinction of biodiversity. In contrast to many other natural resources and because of their informational nature, genetic resources are not endangered by over-exploitation but by other environmentally destructive practices against which they must be actively protected. It can thus be argued that distributive justice for genetic resources concerns not only the distribution of benefits but also the

[6] Although many authors acknowledge the informational nature of genetic resources (e.g. Vogel, 1994; Millum, 2010; De Jonge, 2011; Tvedt and Schei, 2013; Ruiz Muller, 2015; Deplazes-Zemp, 2018b), the definition of genetic resources in the CBD refers to „genetic material of actual or potential value" and there is some controversy on how this should be interpreted (Tvedt and Schei, 2013).

[7] Annex to the Nagoya Protocol (p. 24) available at: https://www.cbd.int/abs/ (accessed May 2019).

costs for biodiversity protection. In other words, not only goods but also bads associated with genetic resources should be distributed fairly (Deplazes-Zemp, 2019).

COMMUTATIVE JUSTICE

Commutative justice is also called "justice in exchange" because it concerns a fair exchange of items or services with the goal of achieving equivalence between giving and receiving (Schroeder and Pogge, 2009; Schroeder and Pisupati, 2010; De Jonge, 2011; Deplazes-Zemp, 2018a). In situations where goods are not exchanged for other goods but where products or services are exchanged for money, this leads to the discussion of just prices or just compensation, and is thus an important principle in the economic context (Koslowski, 2001). The "Fairtrade" label, for instance, symbolizes the aim of generating more commutative justice in economic exchange between farmers in low-income countries and companies in the industrialized world. One of the great challenges in this justice dimension is to determine under what conditions both sides contribute equivalents to the exchange if they are of a different nature. To deal with these substantial difficulties, commutative justice is sometimes also understood in a more procedural sense, according to which an exchange is considered just if both parties voluntarily consent to the transaction procedure employed (Schroeder and Pisupati, 2010). In this case, an overstated price could be considered to be just as long as the buying party pays it voluntarily. Such an interpretation of commutative justice overlaps with the dimension of procedural justice that this article addresses later.

Commutative Justice for Genetic Resources

An ABS system for genetic resources can be understood as a mechanism to deal with the demands of commutative justice. ABS regulates how benefits should be shared *in exchange for* access to genetic resources (Schroeder and Pogge, 2009; Schroeder and Pisupati, 2010; De Jonge, 2011; Deplazes-Zemp, 2018a).[8] The existing focus on the commutative aspect in ABS has been criticized not only because it cannot account for the complexity of justice issues at stake but also because it introduces a clear separation between providers and users of genetic resources. Critics highlight that this does not reflect the real world, where genetic resources are also being used in so-called provider countries (particularly threshold countries) and where it is thus not possible to draw a clear line between the two categories (Korthals and De Jonge, 2009; Nijar et al., 2016). Moreover, it again seems to be the informational nature of genetic resources that complicates the application of commutative justice schemes, which have been developed for material goods. Although it may be relatively straightforward to determine the provider of a material natural resource, such as a barrel of petrol, this is much more difficult in the case of genetic resources, which may have travelled a long distance in the form of a small material sample, an extract or even as a digital sequence before they are actually being used. This means that not only must resource access be controlled for actual users but any removal of minimal quantities of genetic resources, even for non-commercial purposes, must be monitored because they might be used as resources in the future (De Jonge, 2011). I suggested elsewhere that the informational nature of genetic resources is also responsible for another difficulty with ABS achieving commutative justice. We need to ask ourselves what it is that is actually being exchanged in ABS, who has claims on the exchanged goods, and how the claimant can be appropriately compensated (Deplazes-Zemp, 2018a). Does the provider state from the territory of which, for instance, a plant sample has been extracted, really have particular claims on this plant as a genetic resource? It is certainly true that the users of genetic resources gain from information in nature and it seems to be a legitimate request that they give something back in exchange for these free benefits. However, one may wonder whether provider states really are the appropriate recipients of such compensation or whether it should go, for example, directly to biodiversity protection projects, which preserved valuable genetic resources.[9]

Another interesting topic with regard to commutative justice is ABS for traditional knowledge associated with the use of genetic resources. If, for instance, a company uses the knowledge of an indigenous community about a particular health benefit of a plant, this knowledge is also subject to access and benefit-sharing negotiations. It can be argued that, from a commutative justice point of view, it makes a difference whether compensation is demanded in exchange for traditional knowledge or for providing access to a plant growing on state territory. Whereas in the latter case extensive claims on genetic resources might be difficult to legitimize, this is different for the case of traditional knowledge and likewise for domesticated plants. In these cases, the respective communities provide their intellectual good or the products of their work. This distinguishes their claims on this knowledge or plants from that of other communities. It can thus be reasoned that if communities provide such knowledge or breeding efforts, they have good reasons supported by commutative justice to demand compensation (Deplazes-Zemp, 2018a).

[8] The "fair and equitable" clause could be read as another indication of a connection to commutative, since the term "equity" has been used to describe the aim of commutative justice (Adams, 1963; Cook and Hegtvedt, 1983).

[9] The idea that those who use information in nature should pay compensation for the resulting benefits indicates that there is another justice aspect that could be considered in the context of plant genetic resources, namely ecological justice. Nicholas Low and Brendan Gleeson contrast ecological justice with environmental justice by explaining that the latter deals with "conflicts among humans over nature" whereas ecological justice deals with conflicts "between humans and nature" (Low and Gleeson, 1998: p. 49 emphasis in the original). Ecological justice is thus concerned with justice towards the non-human world (Schlossberg, 2007) which is beyond the scope of this article. Whereas on an ecological justice perspective, just compensation for information in nature would require giving something back to nature, I understand just compensation for natural information here as a compensation for those human communities who actively protect biodiversity.

JUSTICE AS RECOGNITION

Justice as recognition is concerned with giving respect and recognition to every person.[10] This means that each human being should be recognized for his or her equal moral status which at the same time implies that each person is respected for his or her individuality and differences to the norm (Taylor, 1992). Justice as recognition emphasizes that we *owe* recognition to others and that withholding recognition is a form of injustice. Feminists, racial movements, and multiculturalism are examples of political struggles for recognition. The importance of recognition has been supported by different philosophical arguments. For instance, Axel Honneth and Charles Taylor emphasize that recognition is a basic human need required for identity formation (Taylor, 1992; Honneth, 1995; Fraser and Honneth, 2003). Nancy Fraser suggests that lack of recognition violates the moral principle of "participatory parity" and is, therefore, unjust (Fraser, 2000; Fraser, 2001; Fraser and Honneth, 2003).

Justice as recognition is, besides distributive justice, another focus in the discourse on environmental justice (Schlossberg, 2007; Walker, 2012). As mentioned above, poor and minority communities often endure more environmental burdens such as waste dumpsites, toxic emissions, or other contaminations than privileged groups. In these cases unjust distribution usually occurs together with misrecognition of these groups who are being discriminated against and not given equal status in society. To achieve environmental justice, it is thus not enough to ensure fair distribution of risks and benefits; rather, it is also necessary to grant just recognition to members of different communities.

Justice as Recognition for Genetic Resources

Even though in the philosophical literature on genetic resources the term "recognition justice" rarely appears, this dimension of justice also plays an important role.[11] The framing of ABS as a system that mediates between providers of genetic resources in the "Global South" and users in the "Global North" indicates that the addressed injustice has also to do with political, economic and cultural power relations at the global level. Although the division between users in the "North" and providers in the "South" is an oversimplification, it is often used in the literature to refer to an unjust tendency. Industrialized countries often located in the "North" tend to profit from genetic resources, whereas biodiversity-rich countries mostly in the "South" are expected to protect genetic resources as biodiversity. This situation is not only unjust from the point of view of distributive justice and commutative justice as discussed above but the North–South interactions in the context of genetic resources also concern justice as recognition. This justice dimension is violated when the "North" takes advantage of historical power relations associated with economic and political privileges. In such cases, users of genetic resources tend to decide when and how to access which genetic resources without respecting providers as equal partners nor considering their customs, culture, or values. This type of misrecognition not only occurs in North–South interactions but also within provider states, when governments do not respected cultures or rights of minority groups. To prevent such misrecognition at global and local level, CBD, NP, and ITPGRFA explicitly acknowledge rights and claims of indigenous and local communities. It has been argued that more attention should be paid to justice as recognition in the context of biodiversity conservation to consider cultural differences (Martin et al., 2016; Robinson and Forsyth, 2016). For instance, certain communities object to the idea of patenting life (Tauli-Corpuz, 2003; Robinson, 2010). To offer them a share in benefits associated with patents on genetic resources misrecognizes their values and world view. Bram De Jonge discusses these issues under the heading of "cognitive justice," which he defines as concerning the "recognition of the plurality of knowledge systems" (De Jonge, 2011: p. 135). I decided to use the concept of "justice as recognition" rather than "cognitive justice" not only because of the former's philosophical tradition and its use in the environmental justice literature but also because, in my view, to recognize the individuality of others goes beyond acknowledging the cognitive aspect of different world views. The notion of recognition justice emphasizes the importance of a respectful attitude by the more powerful. As mentioned above, a similar idea is found in the notion of upstream benefit-sharing, which Bram de Jonge and Michiel Korthals include in their broader conception of distributive justice (De Jonge and Korthals, 2006; Korthals and De Jonge, 2009).

REPARATIVE JUSTICE

I use the term "reparative justice" for the notion that redress is owed to those who suffered injustice in the past. In the literature, this dimension of justice is discussed under different related terms with sometimes overlapping and sometimes clearly distinct meanings (Daly and Proietti-Scifoni, 2011). Particularly in the legal context, the concept "retributive justice" is used for just punishment of those who committed injustice (Boersama, 2011; Daly and Proietti-Scifoni, 2011). This concept thus concentrates on the appropriate punishment of the offenders for the wrongs that they committed. In contrast, the term "corrective justice" usually refers to a conception of justice that focuses on the victims and on the just compensation that they should receive for suffered harms (Urban Walker, 2006). There are certain similarities between corrective justice and commutative justice. Both are linked to reciprocity, and both deal with just compensation. However, while the former

[10] It might be objected that when I defined justice in general as meaning to "acknowledge that all human beings have equal moral status and basic moral rights" (see above) this already involves recognition, which thus is a precondition of all dimensions of justice. It is true that in order to be able to enter a justice relationship with someone and to identify injustices of any type I must recognise the other as having moral status and basic rights. However, there are cases of injustice, where none of the other justice dimensions have been violated but the injustice lies in a form of misrecognition, for instance cases where someone's belief, culture or the like are not being respected. These cases where misrecognition per se is the injustice are discussed here under the heading of "justice as recognition." The possibility that some form of basic misrecognition also underlies other types of injustice does not make it redundant to introduce a separate justice dimension of justice as recognition in order to account for the different types of injustice that can occur in practice.

[11] The following articles are exceptions in the sense that ABS is explicitly discussed in relation to environmental justice including recognition justice: (Vermeylen and Walker, 2011; Martin et al., 2013; Morgera, 2015; Martin et al., 2016).

concerns simultaneous exchange procedures, the latter is backward-looking and concerns compensation for something that happened in the past. "Restorative justice" is a third reparative justice concept besides "retributive justice" and "corrective justice." Authors who use this concept highlights that righting injustice requires more than the remedy of harms: the important aim is to re-establish the relationship between victim and offender, usually in a relatively informal process, and to prevent that same type of injustice recurring in the future. Criminal trials are typically not seen as apt processes to establish restorative justice. Instead, reconciliation or mediation procedures are implemented in which offenders and victims meet, find the truth, and negotiate potential reparations (Johnstone and Van Ness, 2007; Marshall, 1999). Reparations in this sense are not necessarily material but can also consist of a formal apology (Urban Walker, 2006; Sharpe, 2007). A famous example of such a procedure was the Truth and Reconciliation Commission that was set up to address injustices committed during the apartheid era in South Africa. The importance that is given to establishing a relationship of mutual respect connects to "justice as recognition" described above. This illustrates once more how the different dimensions of justice overlap.

When I refer to "reparative justice," I use it as an umbrella term to cover retributive justice, corrective justice, and restorative justice,[12] with the idea that all of these aspects may play a role in righting injustice that took place in the past. In the environmental context, reparative justice, for instance, plays a role in climate justice, when it comes to the "polluter pays" principle (Caney, 2006; Caney, 2010). In Simon Caney's words, this principle suggests that "those who caused a problem[…] should foot the bill" (Caney, 2006: p. 752). This can be understood as a demand for corrective justice, meaning that the polluters are responsible for repairing the damage that they caused. Maybe the "polluter pays" principle could also be interpreted as an example of retributive justice, particularly when one of the discussed objections to the principle is that the polluters were not aware of the effects of their actions and thus should not be the ones who pay (Caney, 2010). Based on that view, it would not be just to *punish* people for something that they caused unintentionally.

Reparative Justice for Genetic Resources

Reparative justice is *not* a predominant justice dimension behind the notion of ABS for genetic resources. Doris Schroeder and Balakrishna Pisupati suggest that while distributive and commutative justice are directly relevant for ABS, reparative justice only plays a role in cases of non-compliance with the protocol which would trigger punishment and repair measures (Schroeder and Pisupati, 2010). However, the reparative justice dimension may still be relevant to understand why and how ABS systems have been implemented. The aim and need to redress some of the historical wrongs that were perpetrated—generally speaking—by the "Global North" against the "South" could be an underlying political motivation for establishing ABS systems. During colonial times, citizens of many biodiversity-rich states in the "Global South" suffered exploitation, oppression, subordination and disrespect, which amounts to injustice at the distributive, commutative and recognition dimensions. It cannot be denied that today colonial-like power relations still persist when the "North" exerts its strong political, cultural, and economical influence on the "South" accompanied by the same type of justice violation known from colonial times. From such a perspective, acknowledging biodiversity-rich states' sovereignty over genetic resources could be understood as an acknowledgment of past misconduct as well as a commitment to consider the interests of less affluent countries in the future. That ABS systems are related to historical injustice has also been described by Jorge Cabrera Medaglia when he wrote: "The roots of ABS can be traced to colonialism and efforts by colonial powers to gain control of the trade in key commodities such as rubber, tea, and cinchona for their own benefit, with little regard for the communities and economies from which these resources originated" (Medaglia, 2015: p. 196). Moreover, Elisa Morgera highlighted that reparative justice played a role in the negotiations of the NP, when the African group demanded that benefit sharing should be extended to genetic resources which are available in *ex situ* collections, i.e., ones that had been exported from the country of origin in the past (Morgera, 2015: pp. 11–12).

PROCEDURAL JUSTICE

The term "procedural justice" has been used in a wider and a narrower sense. According to the former, this dimension of justice is concerned with any type of procedure that leads to a just outcome judged by criteria of other (substantive) justice dimensions. The narrower sense of procedural justice plays an important role in environmental justice, where procedural justice is discussed as the third central justice dimension besides distributive justice and justice as recognition (Schlossberg, 2007; Walker, 2012; Bell and Carrick, 2018). In this narrower sense, procedural justice concerns decision procedures and is achieved if the voice and interests of all involved parties are being considered. Because environmental justice was first the program of a social movement before it became a theoretical field of study, this procedural aspect has been particularly pivotal. One of the main aims of the movement was the empowerment of affected communities. Participatory approaches as a means for just procedures in decision making thus play an important role.

As for other justice dimensions different principles of justice have also been suggested for procedural justice. Derek Bell and Jayne Carrick distinguish three conceptions of procedural justice in the environmental justice discourse, which focus on three alternative principles (Bell and Carrick, 2018). The first principle is *political equality* according to which all affected parties should have an equal voice in the sense of equal power in environmental decision making (Bell and Carrick refer to: Shrader-Frechette, 2002). As an alternative, the principle of *proportionality* emphasizes that power in decision making should reflect the relative stake of the involved parties in the outcome of the decision (Bell and Carrick refer to: Bell and Rowe, 2012). The third conception of procedural

[12] Some conceptions of restorative justice seem not to be covered by my concept of "reparative justice". For instance, what Johnstone and Van Ness call, the "encounter conception of restorative justice", which emphasizes the importance of the encountering process rather than the aim of redressing those who suffered injustice (Johnstone and Van Ness, 2007).

environmental justice introduced by Bell and Carrick is based on the principle of *plurality*. Advocates of this principle criticize procedural justice conceptions emphasizing equality because they suppress difference, but it is argued that just procedures should consider differences in perspectives or interests. This is the same argument that is invoked in the literature on justice as recognition. Although the three principles for just procedures are discussed as three alternative ideals in the theoretical discourse, in practical environmental decision making they are combined in participatory approaches (Bell and Carrick, 2018).

Procedural Justice for Genetic Resources

A focus on fair decision procedures is particularly relevant in the context of genetic resources because, as mentioned earlier, political and economic power between providers and users are often unequally distributed, which is a violation of recognition justice and/or distributive justice. Just decision procedures are thus not only an aim in themselves but also an approach to achieve more justice along other dimensions. The NP addresses some of these problems, for instance by highlighting rights of indigenous and local communities or by requesting scientific and technological collaboration (NP, Article 23). Moreover, one article of the NP is dedicated to capacity-building, it requires that all parties should cooperate in the endeavor of ensuring that also less affluent parties have the capacities to engage in the outlined ABS procedure (NP, article 22). Prior Informed Consent (PIC) and Mutually Agreed Terms (MAT) are two procedural requirements in the NP. Users of genetic resources must obtain PIC from providers.[13] In response, the providers can authorize access to the resource under the condition that MAT are negotiated. Besides the conditions for the access to genetic resources MAT also determine the benefits that will be shared (Greiber et al., 2012; Biber-Klemm and Martinez, 2016). From a procedural justice point of view, these two elements should be implemented with a focus on the principles of political equality, proportionality and/or plurality. To what extent the procedure is participatory and considers these principles, particularly also concerning involvement of indigenous and local communities, depends not only on the users but also the provider states. Therefore, there is a considerable leeway to consider more or less procedural justice within the legal framework.

JUSTICE CHALLENGES IN USING GENETIC RESOURCES

In the article so far, I have attempted to show that all of the introduced dimensions of justice play a role in the context of ABS for genetic resources. In the following, I will discuss three particular justice challenges that arise in the use of plant genetic resources: first, biopiracy; second, environmental burdens from biodiversity conservation; and third, plant genetic resources in agriculture. These examples should illustrate the role that different justice dimensions play in the discourse and how they are being addressed or overlooked. In the course of this analysis, it will become evident that justice challenges must be addressed at two different levels: on the one hand the *institutional level,* which is represented by national and international policy; and on the other hand, the *individual project level,* which concerns specific projects of resource use with their respective ABS negotiations.

CHALLENGE 1: BIOPIRACY

To explain which types of injustice the ABS scheme of the CBD addresses, authors frequently invoke the problem of biopiracy (e.g. Kamau et al., 2010; Millum, 2010). The term refers to unauthorized use of genetic resources or traditional knowledge in the development of a product. Those accused of biopiracy did not share any benefits, recognition or material profit with the community that provided the resources or knowledge in question. Particularly when traditional knowledge is involved, biopiracy is a violation of commutative justice because the providers of this knowledge made an essential contribution to the final product, for which they were not compensated. However, biopiracy is not only a violation of commutative justice. When traditional knowledge was used without the consent of the community, justice as recognition was also violated, because the members of the community were not respected as equal negotiation partners and their rights to their cultural heritage were not acknowledged. One of the aims of ABS in the CBD and NP was to address this type of commutative injustice and misrecognition by introducing just procedures with the requirement for PIC and MAT not only for the export of genetic resources but also for the use of traditional knowledge.

However, using the famous case of the Hoodia cactus, Saskia Vermeylen and Gordon Walker showed that the implementation of an ABS agreement alone does not automatically warrant recognition justice or procedural justice. The succulent plant *Hoodia gordoniiwa* was used as an appetite suppressant by the San, a hunter-gatherer community in southern Africa. In 1996, scientists of the South African Council for Scientific and Industrial Research (CSIR) isolated and patented the active compound of *Hoodia*, without involving the San or acknowledging their active contribution. Eventually, under external pressure, the CSIR eventually got in touch with the San, recognized their contribution, and in 2003 the CSIR and the South African San Council signed a benefit-sharing agreement (Beattie, 2005; Wynberg, 2005; Vermeylen and Walker, 2011). Even though the CSIR obtained PIC by the official representatives of the San, Vermeylen and Walker doubt that this was a case of procedural justice. In some places, the process was not really participatory because most group members were not aware of it. Moreover, the San did not receive enough legal and strategic assistance in the negotiation process and their opinion was not really taken into account. Vermeylen and Walker further cite the Hoodia Benefit-Sharing agreement as a case of violation of justice as recognition, which requires not only recognizing the other party as a partner with equal status and rights but also acknowledging and considering differences in culture and political tradition (Vermeylen and Walker, 2011). The San are known as an egalitarian community that functions without formal political institutions and

[13] PIC implies that before accessing the resource in question, the potential user must provide all the relevant information on the intended utilization project, including the conditions of access as well as the intended use.

power hierarchies, but with decision making processes that involve consensus procedures. Even if the PIC and MAT procedures had been performed according to liberal democratic Western ideals, they would have been inflicted on this community against its own political tradition and values, because only a selection of representatives where involved in the negotiations.

Finally, in the *Hoodia* example, reparative justice also plays a role. As mentioned above, the CSIR originally patented the active compound in *Hoodia* without involving the San, and it acknowledged their contribution only under external pressure. The San thus had been wronged and the question is whether it is enough to ensure commutative, recognition and procedural justice in the future or whether, in addition, material or symbolic reparation would be appropriate.

CHALLENGE 2: ENVIRONMENTAL BURDENS FROM BIODIVERSITY CONSERVATION

The second justice challenge in the context of plant genetic resources concerns the background against which the ABS system has been developed in the CBD. The CBD has three main objectives, first, the conservation of biodiversity; second, the sustainable use of its components; and third, the fair and equitable sharing of benefits from genetic resources. The first objective places high demands on biodiversity-rich countries, which at the same time are often low-income countries in the "South" that struggle with poverty. The second objective, too, addresses particularly this group of countries, because industrialized countries in the "North" already went through industrial development, albeit in a non-sustainable way. It thus seems that the "Global South" carries a disproportionate burden when it comes to biodiversity conservation, even if affluent countries cover some of the conservation costs. Biodiversity-rich countries are affected, for instance by opportunity costs resulting from the requirement to setup protection areas which implies that communities living on that land waive the right to cultivate it. Other burdens associated with conservation projects include the displacement of local communities to restrict human influence on the respective area (Agrawal and Redford, 2009). In that sense, the burden of biodiversity conservation is not distributed justly. What makes this distributive injustice more pronounced is that benefits from the use of genetic resources, directly attributable to the effort of conserving biodiversity, tend to flow into the "Global North". The request to ensure that the "South" also gets a share in benefits could thus be understood as a means to achieve more distributive justice. I suggest elsewhere that mitigation of the unfair distribution of burdens and benefits from biodiversity could be linked through a global biodiversity fund, which would be supported by those who benefit from genetic resources and would be disbursed for biodiversity conservation projects (Deplazes-Zemp, 2019). Interestingly, the Multilateral System of the ITPGRFA has established a similar type of fund financed by benefits from genetic resources and is used to support projects in conservation or development of agriculture. However, as will be elaborated below, the fund of the Multilateral System was not primarily set up with the aim to ensure fair distribution of the burden of biodiversity conservation but to ensure food security. These distributive justice issues could be implemented at the institutional level, but when it comes to individual ABS negotiations, genetic resource users could also acknowledge this issue, for instance by contributing directly to justly designed biodiversity conservation projects in the provider country.

The idea that those who profit from biodiversity, for instance in bioprospecting projects, contribute to biodiversity conservation can also be understood as a requirement of commutative justice. Based on this view, the contribution would be understood as a form of compensation for the possibility to benefit from genetic resources, which persisted thanks to biodiversity conservation (Deplazes-Zemp, 2018a).

Justice as recognition is important in this context too. It is necessary to recognize and consider the differing values, norms and needs of the contracting parties to be able to understand burdens associated with biological conservation, as well as the benefits that could be shared. Being open to other world views may involve, for instance, calling into question our own understanding of biodiversity and nature as opposed to humanity (De Jonge, 2011; Martin et al., 2013).

Finally, at least at the institutional level the dimension of reparative justice also plays a role when it comes to the connection between ABS for genetic resources and environmental burdens. That biodiversity is threatened today is to a large degree a consequence of the lifestyle and unsustainable development in the "Global North". With reference to reparative justice, one might thus reason for a "destroyer pays" principle analogous to the "polluter pays" principle in the context of climate justice. Moreover, biodiversity conservation may also have a colonial legacy, because important national parks were established for the benefit of colonial rulers without any consideration for traditional culture and lifestyle (Chan and Satterfield, 2013). Even if current ABS negotiations may not be the right occasion to repair these historical injustices, awareness and acknowledgment of the need for reparative justice may help to understand and respect the situation of communities and states in biodiversity-rich regions.

CHALLENGE 3: PLANT GENETIC RESOURCES IN AGRICULTURE

Plant genetic resources used in agriculture pose additional justice challenges to other types of genetic resources. In the following I will emphasize the role of the different dimensions of justice in these particular challenges. One of the differences between plant genetic resources in agriculture and, for instance, genetic resources of plants in the rainforest, is that agricultural plants are not purely natural (e.g., Halewood et al., 2013; Deplazes-Zemp, 2018b). They are domesticated, meaning that they are the result of breeding processes in which humans shaped crops over centuries. In contrast to purely natural resources, domesticated plants were generated by certain communities, farmers, and breeders or more recently by scientists in companies, who thus have particular claims on these plants. In that sense, a demand to distribute benefits from these resources equally among

everybody (those who contributed to the plant and those who did not do so) seems to be more difficult to legitimize. Farmers or breeders who "improved" these plants can appeal to commutative justice and argue that if they make these plants available, their effort and creativity should be acknowledged and compensated (Deplazes-Zemp, 2018a; Deplazes-Zemp, 2018b). Intellectual property rights (IPR), such as patents and plant breeders' rights, have been used as mechanisms to implement such compensation by ensuring that only the holders of these rights are entitled to commercially benefit from the plant in question. Although these property rights may be well suited to acknowledging the contribution of scientific innovation of commercial breeders in industrialized countries, they are unsuitable to account for the collective contributions of small-scale farmers in low-income countries, where the use and generation of novel varieties go hand in hand and cannot be assigned to individual breeders who put the crop on the market at one particular moment (Borowiak, 2004; Correa, 2015; Oguamanam, 2018; Adebola, 2019). IPR over plant genetic resources, thus, raise a variety of justice issues. They fail to achieve commutative justice because farmers with particular claims on these resources cannot profit from the IPR system. Moreover, this is also a case of misrecognition. IPR fail to take into account agricultural practices of farmers in low-income countries. Consequently, not only the particular contributions of these farmers to valuable agricultural plants are being misrecognized but also the claims that these communities have on their products and their particular interests to be compensated if their products are being used. To correct these commutative and recognition injustices toward small-scale farmers, the concept of "farmers' rights" was brought into the discourse to account for the generation of new varieties by farmers and grant them certain rights over these plant genetic resources (Borowiak, 2004). The ITPGRFA was the first international binding treaty that explicitly recognized farmers' rights; in addition, the literature also discussed ABS as outlined in the CBD and NP as an approach that allows accounting for farmers' contributions *via* PIC and MAT (Correa, 2015; Oguamanam, 2018; Adebola, 2019).

How different dimensions of justice come together and may lead to different expectations in case of plant genetic resources in agriculture can also be illustrated with the previously mentioned Multilateral System of the ITPGRFA. The Multilateral System provides facilitated access to 64 of the most important crops and requires that those who accessed genetic resources through this system will freely share resulting benefits or pay a percentage of their profits into a common fund.[14] Agricultural plant genetic resources covered under the Multilateral System can be accessed without obtaining PIC and negotiating MAT but by using a standard template the "Standard Material Transfer Agreement" (SMTA) negotiated by the Parties to the ITPGRFA. However, since benefits from the use of these resources do not flow to the provider but to the Multilateral System as a third party, none of the contracting parties have a particular interest in monitoring compliance with the SMTA. To address this problem, the concept of the "Third-Party Beneficiary" has been introduced into the SMTA. The parties to the SMTA agree that the Third-Party Beneficiary has certain rights, for instance, to monitor compliance with the agreement (Manzella, 2013; Moore, 2013).

Analyzed from the stance of the different dimensions of justice, the problem of compliance with the SMTA arises because of the combination of two justice dimensions. An agreement between providers and users of genetic resources usually aims at implementing commutative justice by ensuring that the exchange is fair. In contrast, the Multilateral System supports distributive justice ensuring that the possibility to access and benefit from these resources is distributed fairly and recognition justice in the sense of recognizing basic rights to food. These aims can, however, not be secured by a procedure that involves only two "self-interested" negotiation parties. The introduction of the Third-Party Beneficiary can thus be understood as a means ensure distributive or recognition justice in a commutative justice framework.

As just indicated, the Multilateral System points to another, more fundamental, ethical challenge raised by agricultural plant genetic resources, which has to do with the role of agriculture in the production of staple foods and in ensuring food security (De Jonge and Korthals, 2006). Safeguarding this role of agricultural genetic resources was the main motivation to provide facilitated access to the 64 crops covered under the Multilateral System. Food is a basic good that people need for health and well-being, therefore, an understanding of humans as beings with basic moral rights implies the duty of ensuring food security. This aim goes beyond what is demanded by a classical natural resource oriented understanding of distributive justice.[15] While the latter demands fair distribution of *existing* goods, the basic moral right to food necessitates safeguarding that enough food is available. This can lead to a positive duty to ensure that food can be produced also, for instance, under changed climatic conditions.[16]

Recognition justice is also relevant in this context, when it is demanded that every person's moral right to food must be acknowledged with consideration for varying needs and interests. Bram de Jonge pointedly describes how there is a certain type of tension between this basic moral requirement of ensuring food security[17] and commutative justice (De Jonge, 2011). Although the first moral requirement suggests that farmers or breeders who develop new staple foods should make them available to everybody, the latter demands that they be compensated for their products. However, from the identification of such a tension it does not follow that one of the moral requirements must be prioritized. Instead, the situation can be understood as the challenge to find solutions to implement both moral demands. This challenge cannot only be addressed at the institutional level by drafting all-encompassing

[14] The Multilateral System: http://www.fao.org/plant-treaty/areas-of-work/the-multilateral-system/overview/en/ (accessed May 2019).

[15] This may not apply to a less traditional conception of distributive justice associated with the notion of "upstream benefit-sharing" suggested by Bram de Jonge and Michiel Korthals. According to this understanding distributive justice needs to focus on a globally more just distribution of opportunities to set the research and innovation agenda. This could lead to a prioritization of the positive duty of ensuring that food resources are being generated where they are scarce (De Jonge and Korthals, 2006; Korthals and De Jonge, 2009).

[16] An according duty could have been a motivation to facilitate, and thereby encourage, access to the 64 most important crops for farmers, breeders and researchers in the Multilateral System.

[17] De Jonge speaks of a "principle of need and equity" (De Jonge, 2011: p137f).

regulations; it must also be addressed at the individual project level, by acknowledging and rewarding contributions to agricultural plants even when this may not be explicitly required by the regulatory scheme.

The purpose of this section was to illustrate that usually more than one justice dimension is concerned in justice challenges involving plant genetic resources. This insight can be practically relevant for at least three reasons.

First, too narrow a focus on one dimension of justice may lead to unsatisfying results, because injustice at other dimensions persists, for instance, if biopiracy is seen exclusively as a violation of commutative justice and aspects of justice as recognition or reparative justice are being ignored. Although PIC and MAT may suffice to warrant commutative justice as defined in a Western context, justice as recognition requires considering potential conflicts of values between the involved parties. Consequently even our own principles of procedural justice may need reflection as described in the case of negotiations with the San above. The problems with benefit sharing as part of the Multilateral System also indicated that the focus on only one dimension of justice is not sufficient. A procedure that was constructed to deal with commutative justice needs adaptation to be able to address aims of distributive justice or recognition justice.

Second, tensions may arise between the different justice dimensions. For instance, certain parties highlight that plant genetic resources in agriculture are cultural products and those who developed them have special claims on benefits, which need to be considered by commutative justice. Others, however, highlight that as resources relevant for food security, plant genetic resources should be freely available and subject to distributive or recognition justice. The previously mentioned biopiracy case involving the San also reveals tensions between an ideal of procedural justice and justice as recognition. In certain cases, this type of tension may lead to difficult ethical dilemmas, for instance, when a community for traditional reasons does not agree to involve women or young people in decision procedures. Should their culture be respected or should the participatory ideals of procedural justice be implemented?[18]

Third, the focus on different justice dimensions may lead to different expectations in negotiation processes. In the discussed biopiracy case, the companies understood their task in the first place in the sense of commutative justice as providing compensation. However, the San also expected to be recognized. Although officially ABS systems are drafted to achieve commutative justice at the level of individual projects, certain stakeholders also seem to expect that such a system establishes distributive justice at a global and international level.

CONCLUSIONS

In this article, I introduced five dimensions of justice that play a role in dealing with plant genetic resources in "wild" nature and agriculture, namely distributive justice, commutative justice, justice as recognition, reparative justice, and procedural justice. I then analyzed how these dimensions meet and overlap in some of the major justice challenges faced in the context of plant genetic resources. The article aims at giving some insight into why the use of genetic resources generates so much controversy and into what needs to be considered in regulating and handling them justly. I will respond to these aims with two conclusions for a just use of plant genetic resources.

First conclusion: Justice challenges posed by the use of plant genetic resources are multi-faceted and cannot be addressed by focusing exclusively on one dimension of justice. The analysis of the literature shows that different authors concentrate on different justice-related questions raised by genetic resources. I presented these different questions along the five introduced dimensions of justice. They often overlap, but to reduce the justice challenges to one or two of these dimensions would not do justice to the complexity of practical issues. Assuming that all of the justice dimensions are strong moral demands, we thus need to account for each dimension and consider how we can address them together when we work toward more fairness and equity in dealing with plant genetic resources.

Second conclusion: Because justice challenges are multi-faceted, they cannot be met at the institutional level alone, but the challenges must be identified and addressed for each case individually. This overview article indicates that existing institutional ABS frameworks can be used to address several of the justice challenges, but at the same time these regulatory frameworks seem not sufficient to meet the challenges. Therefore, it is particularly important that the individual users of genetic resources, including researchers who work in non-commercial projects, are also aware of the issues at stake and find individualized solutions to address them. There is a risk that the increasing administrative burden associated with ABS obscures the actual justice issues at stake. However, losing sight of these issues at the project level would certainly work against the aim of increasing fairness and equity in ABS for plant genetic resources.

AUTHOR CONTRIBUTIONS

AD-Z wrote this article alone and is responsible for the literature search, the structure and design of the article, as well as the content and argumentation.

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[18] Usually, it is held that recognition justice cannot justify the violation of basic human rights. In that sense, the United National Declaration on the Rights of Indigenous Peoples (UNDRIP) also requires that indigenous peoples' institutional structures and their procedures need to be "in accordance with international human rights standards" (UNDRIP, article 34, available at https://www.un.org/esa/socdev/unpfii/documents/DRIPS_en.pdf (accessed August 2019)).

REFERENCES

Adams, J. S. (1963). Toward an understanding of inequity. *J. Abnor. Soc. Psychol.* 67 (5), 422–436. doi: 10.1037/h0040968

Adebola, T. (2019). Access and benefit sharing, farmers' rights and plant breeders' rights: reflections on the African Model Law. *Queen Mary J. Intellect. Prop.* 9 (1), 105–121. doi: 10.4337/qmjip.2019.01.06

Agrawal, A., and Redford, K. (2009). Conservation and displacement: an overview. *Conserv. Soc.* 7 (1), 1–10. doi: 10.4103/0972-4923.54790

Armstrong, C. (2017). *Justice and natural resources, an egalitarian theory*. Oxford: Oxford University Press. doi: 10.1093/oso/9780198702726.001.0001

Beattie, A. J. (2005). "New products and industries from biodiversity," in *Ecosystems and human well-being: current state and trends. Findings of the condition and trends working group*. Eds. R. M. Hassan, R. Scholes, and N. Ash (London: Island Press), 273–295.

Bell, D., and Carrick, J. (2018). "Procedural environmental justice," in *The Routledge handbook of environmental justice*. Eds. R. Holifield, J. Chakraborty, and G. Walker (London: Routledge), 101–112. doi: 10.4324/9781315678986-9

Bell, D., and Rowe, F. (2012). Are climate policies fairly made? Available at: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.569.1307&rep=rep1&typ=pdf (accessed May 2019).

Biber-Klemm, S., and Martinez, S. I. (2016). Utilization of genetic resources and associated traditional knowledge in academic research. A good practice guide for access and benefit-sharing. *Swiss Academy of Sciences*. Available at: http://www.naturwissenschaften.ch/service/publications/79736-utilization-of-genetic-resources-and-associated-traditional-knowledge-in-academic-research (accessed May 2019).

Boersama, D. (2011). "Retributive justice," in *encyclopedia of global justice*. Ed. D. K. Chatterjee (Netherlands: Springer), 952–954. doi: 10.1007/978-1-4020-9160-5_381

Borowiak, C. (2004). Farmers' rights: intellectual property regimes and the struggle over seeds. *Politics Soc.* 32 (4), 511–543. doi: 10.1177/0032329204269979

Bullard, R. D. (1993). The threat of environmental racism. *Nat. Resour. Environ.* 7 (3), 23–2655–56.

Caney, S. (2006). Cosmopolitan justice, responsibility, and global climate change. *Leiden J. Int. Law* 18, 747–775. doi: 10.1017/S0922156505002992

Caney, S. (2010). Climate change and the duties of the advantaged. *Crit. Rev. Int. Soc. Political Philos.* 13 (1), 203–228. doi: 10.1080/13698230903326331

Chan, K. M. A., and Satterfield, T. (2013). "Justice, equity, and biodiversity," in *Encyclopedia of Biodiversity*. Ed. S. A. Levin (Amsterdam: Elsevier), 434–441. doi: 10.1016/B978-0-12-384719-5.00252-5

Cook, K. S., and Hegtvedt, K. A. (1983). Distributive justice, equity, and equality. *Annu. Rev. Sociol.* 9, 217–241. doi: 10.1146/annurev.so.09.080183.001245

Correa, C. M. (2015). Plant variety protection in developing countries. *Association for Plant Breeding for the Benefit of Society (APBREBES)*. Available at: http://www.apbrebes.org/files/seeds/ToolEnglishcompleteDez15.pdf (accessed May 2019).

Daly, K., and Proietti-Scifoni, G. (2011). "Reparation and restoration," in *The Oxford handbook of crime and criminal justice*. Ed. M. Tonry (Oxford: Oxford University Press), 207–253. doi: 10.1093/oxfordhb/9780195395082.013.0008

De Jonge, B. (2011). What is fair and equitable benefit-sharing? *J. Agric. Environ. Ethics* 24, 127–146. doi: 10.1007/s10806-010-9249-3

De Jonge, B., and Korthals, M. (2006). Vicissitudes of benefit sharing of crop genetic resources: downstream and upstream. *Dev. World Bioeth.* 6 (3), 144–157. doi: 10.1111/j.1471-8847.2006.00167.x

Deplazes-Zemp, A. (2018a). Commutative justice and access and benefit sharing for genetic resources. *Ethics, Policy & Environment* 21 (1), 110–126. doi: 10.1080/21550085.2018.1448042

Deplazes-Zemp, A. (2018b). 'Genetic resources', an analysis of a multifaceted concept. *Biol. Conserv.* 222, 86–94. doi: 10.1016/j.biocon.2018.03.031

Deplazes-Zemp, A. (2019). A global biodiversity fund to implement distributive justice for genetic resources. *Dev. World Bioeth.* doi: 10.1111/dewb.12230

Dolzer, R. (2005). Fair and equitable treatment: a key standard in investment treaties. *Int. Lawyer* 39 (1), 87–106. doi: 10.1163/22119000-12340141

Dworkin, R. (2000). *Sovereign virtue: the theory and practice of equality*. Cambridge, MA: Harward University Press.

Fraser, N. (2000). Rethinking Recognition. *New Left Rev.* 3 (3), 107–120.

Fraser, N. (2001). Recognition without Ethics? *Theory Culture Soc.* 18 (2-3), 21–42. doi: 10.1177/02632760122051760

Fraser, N., and Honneth, A. (2003). *Redistribution or Recognition? A Political-Philosophical Exchange*. London, New York: Verso.

Greiber, T., Moreno, S. P., Ahren, M., Carrasco, J. N., Kamau, E. C., Medaglia, J. C., et al. (2012). An explanatory guide to the nagoya protocol on access and Benefit-sharing. *IUCN Environmental Law Centre*. Available at: https://www.iucn.org/content/explanatory-guide-nagoya-protocol-access-and-benefit-sharing (accessed May 2019).

Halewood, M., Lopez Noriega, I., and Louafi, S. (2013). "The global crop commons and access and benefit-sharing laws: examining the limits of policy support for the collective pooling and management of plant genetic resources," in *Crop genetic resources as a global commons, challenges in international law and governance*. Eds. M. Halewood, I. Lopez Noriega, and S. Louafi (London: New York: Routledge), 1–36.

Honneth, A. (1995). *The struggle for recognition: the moral grammar of social conflicts*. United Kingdom: Polity Press.

Johnstone, G., and Van Ness, D. W. (2007). "The meaning of restortive justice," in *Handbook of restorative justice*. Eds. G. Johnstone and D. W. Van Ness (Devon: Willan Publishing), 5–23.

Justinian, Moyle, J. B. (translator). (1913). The Institutes of Justinian. *Project Gutenberg*. Available at: http://www.gutenberg.org/files/5983/5983-h/5983-h.htm (accessed May 2019).

Kamau, E. C., Fedder, B., and Winter, G. (2010). The nagoya protocol on access to genetic resources and benefit sharing: what is new and what are the implications for provider and user countries and the scientific community? *Law Environ. Dev. J.* 6 (3), 246–262.

Korthals, M., and De Jonge, B. (2009). Two different ethical notions of benefit sharing of genetic resources and their implications for global development. *New Genet. Soc.* 28 (1), 87–95. doi: 10.1080/14636770802670308

Koslowski, P. (2001). "Commutative justice," in *Principles of ethical economy.* (Netherlands: Springer), 184–210. doi: 10.1007/978-94-010-0956-0_9

Low, N., and Gleeson, B. (1998). *Justice, society and nature, An exploration of political ecology*. London, New York: Routledge.

Manzella, D. (2013). "The design and mechanics of the multilateral system of access and benefit sharing," in *Crop genetic resources as a global commons, challenges in international law and governance*. Eds. M. Halewood, I. Lopez Noriega, and S. Louafi (London, New York: Routledge), 150–164.

Marshall, T. F. (1999). Restorative justice an overview. *Coventry: Coventry Restorative Justice Forum*. Available at: http://www.antoniocasella.eu/restorative/Marshall_1999-b.pdf (accessed May 2019).

Martin, A., Coolsaet, B., Corbera, E., Dawson, N. M., Fraser, J. A., Lehmann, I., et al. (2016). Justice and conservation: the need to incorporate recognition. *Biol. Conserv.* 197, 254–261. doi: 10.1016/j.biocon.2016.03.021

Martin, A., McGuire, S., and Sullivan, S. (2013). Global environmental justice and biodiversity conservation. *Geog. J.* 179 (2), 122–131. doi: 10.1111/geoj.12018

Medaglia, J. C. (2015). "Access and Benefit-Sharing: North–South challenges in implementing the convention on biological diversity and its Nagoya Protocol," in *International environmental law and the global south*. Eds. S. Alam, S. Atapattu, C. G. Gonzalez, and J. Razzaque (Cambridge: Cambridge University Press), 192–213. doi: 10.1017/CBO9781107295414.010

Millum, J. (2010). How should the benefits of bioprospecting be shared? *Hastings Center Rep.* 40 (1), 24–33. doi: 10.1353/hcr.0.0227

Moore, G. (2013). "Protecting the interests of the multilateral system under the Standard Material Transfer Agreement: the third party beneficiary in *Crop genetic resources as a global commons, challenges in international law and governance* Eds M. Halewood, I. Lopez Noriega and S. Louafi (London, New York: Routledge), 165–177.

Morgera, E. (2015). Justice, equity and benefit-sharing under the Nagoya protocol to the convention on biological diversity. BENELEX Working Paper. Available at: https://ssrn.com/abstract=2610528 (accessed May 2019) (Edinburgh School of Law Research Paper No. 2015/16), 1-23. doi: 10.2139/ssrn.2610528

Nijar, G. S., Louafi, S., and Welch, E. W. (2016). The implementation of the Nagoya Protocol for the research sector: experience and challenges. *International Environmental Agreements: Politics, Law and Economics* (1–15). doi: 10.1007/s10784-016-9328-7

Nine, C. (2012). *Global justice & territory*. Oxford: Oxford University Press. doi: 10.1093/acprof:oso/9780199580217.001.0001

Oguamanam, C. (2018). Plant breeders' rights, farmers' rights and food security: Africa's failure of resolve and India's wobbly leadership. *Indian Journal of Law*

and Technology. Ottawa Faculty of Law Working Paper No. 2018-17. Available at: https://ssrn.com/abstract=3173268 (accessed May 2019).

Rawls, J. (1971, 2005). *A theory of justice*. Cambridge, Mass: Harward University Press.

Robinson, D. F. (2010). Locating biopiracy: geographically and culturally situated knowledges. *Environ. Plann.* 42, 38–56. doi: 10.1068/a41346

Robinson, D. F., and Forsyth, M. (2016). People, plants, place, and rules: the Nagoya Protocol in pacific island countries. *Geog. Res.* 54 (3), 324–335. doi: 10.1111/1745-5871.12178

Ruiz Muller, M. (2015). *Genetic resources as natural information, implications for the convention on biological diversity and Nagoya protocol*. London, New York: Earthscan, Routledge. doi: 10.4324/9781315754451

Schlossberg, D. (2007). *Defining Environmental Justice: Theories, Movements, and Nature*. Oxford: Oxford University Press. doi: 10.1093/acprof:oso/9780199286294.001.0001

Schroeder, D., and Pisupati, B. (2010). Ethics, justice and the convention on biological diversity. *UNEP*. Available at: https://www.unenvironment.org/resources/report/ethics-justice-and-convention-biological-diversity (accessed May 2019).

Schroeder, D., and Pogge, T. (2009). Justice and the convention on biological diversity. *Ethics Int. Aff.* 23 (3), 267–280. doi: 10.1111/j.1747-7093.2009.00217.x

Sharpe, S. (2007). "The idea of reparation," in *Handbook of restorative justice*. Eds. G. Johnstone and D. W. Van Ness (Devon: Willan Publishing), 24–41.

Shrader-Frechette, K. (2002). *Environmental justice: creating equity, reclaiming democracy*. Oxford: Oxford University Press. doi: 10.1093/0195152034.001.0001

Tauli-Corpuz, V. (2003). *Biodiversity, Traditional Knowledge and Rights of Indigenous Peoples*. Penang: TWN Third World Network. Available at: https://www.twn.my/title2/IPR/pdf/ipr05.pdf (accessed May 2019).

Taylor, C. (1992). "The politics of recognition," in *Multiculturalism: examining the politics of recognition*. Ed. A. Gutman (Princeton: Princeton University Press), 25–73.

Tvedt, M. W., and Young, T. (2007). Beyond access: exploring implementation of the fair and equitable sharing commitment in the CBD. *IUCN Environ. Policy Law Paper* 67 (2), 1–148.

Tvedt, M. W., and Schei, P. J. (2013). "The term 'genetic resources' Flexible and dynamic while providing legal certainty?," in *Global governance of genetic resources, access and benefit sharing after the Nagoya protocol*. Eds. S. Oberthür and K. G. Rosendal (New York, London: Routledge), 18–32.

Urban Walker, M. (2006). Restorative Justice and Reparations. *J. Soc. Philos.* 37 (3), 377–395. doi: 10.1111/j.1467-9833.2006.00343.x

Vermeylen, S., and Walker, G. (2011). Environmental Justice, Values, and Biological Diversity: The San and the Hoodia Benefit-Sharing Agreement," in *Environmental inequalities beyond borders: local perspectives on global injustices*. Eds. J. Carmin, and J. Agyeman (Cambridge, Mass.: MIT Press).

Vogel, J. H. (1994). *Genes for sale, privatization as a conservation policy*. New York, Oxford: Oxford University Press.

Walker, G. (2012). *Environmental justice, concepts, evidence and politics*. London, New York: Routledge. doi: 10.4324/9780203610671

Wynberg, R. (2005). Rhetoric, realism and benefit-sharing, use of traditional knowledge of hoodia species in the development of an appetite suppressant. *J. World Intell. Prop.* 7 (6), 851–876. doi: 10.1111/j.1747-1796.2004.tb00231.x

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The Rapeseed Potential in Poland and Germany in the Context of Production, Legislation, and Intellectual Property Rights

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Rapeseed is an essential crop which is used in many different areas as edible oil, biodiesel, lubricant, and feed. It is one of the most popular oil crops in Europe (63% of oilseeds production in 2017). The current study highlights the potential for further rapeseed development in European Union (EU), with special emphasis on Germany (19% of EU production) and Poland (12% of EU production). The study focused on three factors: cultivation area, volume of production and the numbers of Intellectual Property Rights (IPR), particularly patents granted for rapeseed or rapeseed-related inventions and plant variety rights. Possible further obstacles to development, such as current legal framework, were also taken under consideration. The analyzed statistical data shows that both the cultivation area, as well as the volume of production of rapeseed fluctuated in the last decade in both examined countries, while the numbers for European patent publications and Community Plant Variety Rights showed a rising trend, indicating investments in the Research and Development (R&D) of the crop. The data analysis seems to confirm a hypothesis that there is a potential for the development of rapeseed as a versatile, multi-use crop; however, the current EU GMO policies and a legal uncertainty as to the status of products of certain modern gene editing techniques may hamper making optimal use of this potential.

Keywords: agricultural innovation, new breeding techniques, patents, plant variety rights, rapeseed

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INTRODUCTION

Rapeseed has multiple applications viz. human food, cattle feed, and for industrial purposes as a source of biodiesel or bioethanol. Research is being carried out to utilize not only seeds and oil cake (Negahdar et al., 2016; Kdidi et al., 2019) but also other by-products of oil production, such as straw (Wang et al., 2019). Rapeseed production may improve the sustainability of land use, which may also require advancements in the genetic diversity of the plants and hence the development in breeding itself, to achieve efficient use of genetic resources through biological progress. However, certain legal obstacles, in particular after the recent Court of Justice of the EU judgement in the C-528/16 "mutagenesis" case, which seems to limit the choice of breeding methods available to EU

breeders (see sec. 3.3), may hamper this developmental potential and put EU breeders at a disadvantage in comparison to their competitors from other countries.

According to the Food and Agriculture Organization of the United Nations in 2017, the world production of oilseeds (rapeseed, sunflower seed, soybean, linseed) amounted to 479 million tons, whereas consumption amounted to 492 million tons (FAOSTAT, 2018; OECD-FAO, 2018). Soybean had the largest share of oilseed production in the world in 2017 (73%), whereas rapeseed was classified in second place, with a share of 16%.

The European Union (EU) was the world leader in rapeseed production in 2017 (22 million tons). The next places were occupied by Canada (21 million tons), China (13 million tons), India (7.9 million tons), Australia (4.3 million tons), and Ukraine (2.1 million tons) (FAOSTAT, 2018). According to the statistics of the Institute of Agricultural and Food Economics - National Research Institute in Poland (2018), the greatest producers of rapeseed in the EU are the following: France, Germany, Poland, Romania, Great Britain, the Czech Republic, Hungary, Denmark, and Slovakia.

There are different common names of the *Brassica napus* that are well-known for high oil content: rapeseed, rape, canola. The name "canola" is derived from the words "Canada" and "oleo" (oil) and is used to describe rapeseed varieties with low erucic acid and low glucosinolate content in extracted edible oil (Canola Council, 2017). Rapeseed oil is commonly used for cooking, lighting, industrial uses, and feed, especially rapeseed meal and rapeseed cake, which are by-products of oil production. Rapeseed meal contains approximately 36–38% protein and 2–4% fat (Brzóska et al., 2010). Rapeseed cakes are moister than rapeseed meal and contain 10–14% fat. Moreover, rapeseed feeds contain more mineral ingredients than soybean meal (calcium, iron, manganese, phosphorus, magnesium, and selenium) (Woźniak and Twardowski, 2018).

Rapeseed meal is used as valuable feed; however, there are strict limitations concerning the amount used in animal feeding, due to its specific properties (Herkes, 2019). Rapeseed contains glucosinolates, which are the main antinutritional factor that hinders the animal nutrition by making chelates with minerals, which cause unavailability of essential minerals to animals during digestion (Kaczmarek et al., 2016). There is a chance of increasing the share of feed components derived from rapeseed. However, the high fiber content (up to 16%) that affects the digestibility of animals must be highlighted. The fiber content of the seeds and by-products of rapeseed can be reduced through breeding and development of new varieties (Ogrodowczyk and Bartkowiak-Broda, 2013). Canola and rapeseed contain approximately 40% oil. Canola oil is high in oleic acid, which makes it competitive with other cooking oils. Moreover, the oil is also a high-grade lubricant and fuel additive; therefore, conversion to biodiesel is just one of its several potential final uses (Herkes, 2019).

An enterprise can strengthen its market position and gain a competitive advantage through utilization of Intellectual Property Rights (IPR). Such exclusive rights provide a means for obtaining a return on investment in research and development (R&D), through licenses or the transfer of rights. IPR facilitate technology transfers and allow for access to new markets. The monopoly granted by exclusive rights provides owners with an ability to efficiently protect themselves against infringers (Andrews and Criscuolo, 2013). Hence, various forms of IPR are typically obtained by entrepreneurs working in innovative fields. An analysis of numbers of intellectual property rights granted can provide information on R&D investments in a given area of technology (Griliches, 1998).

One of the indicators of development of various industries, including agriculture, is the amount of granted and commercialized patents and the rate of change of this amount. A patent grants an exclusive right to commercially use, distribute, and license the protected invention. The granting of patents, licenses, and other proprietary rights facilitates and triggers company's development; allows it to enter a higher, global level of operation; and can also become an important part of the entity's revenues (European Commission, 2013). A broad patent portfolio may also contribute to the company's market value (Coad and Rao, 2006). Patents are granted by specialized authorities, such as the European Patent Office (EPO) or national patent offices and are listed in publicly available databases, making them relatively easy to research and assess statistically.

In the field of plant breeding, there is also an alternative exclusive right in use, namely the plant variety right, which provides its owner with exclusivity when it comes to commercialization of their variety. Like patents, plant variety rights are granted by a specialized office (e.g., the Community Plant Variety Office—CPVO—in the EU) and are collected in publicly available databases.

The aim of the study was to analyze the potential for development of rapeseed in Europe, with an emphasis on Poland and Germany. The tested hypothesis was that there is indeed a potential for the development of rapeseed as a versatile, multi-use crop. Three indicators were used in the analysis: the overall cultivation area and its changes over time, the volume of production and its changes over time, and the numbers of IPR (patent publications concerning rapeseed and plant variety rights granted) and the changes of those numbers over the years. The choice of those indicators allows to see not only the utilization of the crop but also the dynamics of R&D investments in technologies surrounding it. Additional potentially limiting factors, such as legal obstacles, were also taken into account. Poland and Germany were singled out due to the similarities of their markets, comparable climatic conditions, their mutual co-dependency and strong commercial relations, and due to the fact that they account for over 30% of overall rapeseed production in the EU.

It was not the aim of this study to present IPR as means for increasing the rapeseed potential. The data on patent and plant variety rights were merely used as indicators of the condition and prospects for rapeseed development, alongside other factors, such as cultivation area and legal obstacles.

MATERIALS AND METHODS

The study used research data published by Directorate-General for Agriculture and Rural Development (DG AGRI, 2019)

and Eurostat as well as data from the Central Statistical Office (CSO) of Poland in order to gather data about the land use and production volume of rapeseed and their changes in time.

Patent data can be used as indicators of technological development of multiple areas of technology, including biotechnology (Pilkington et al., 2002; OECD, 2005; OECD, 2008; Dubarić et al., 2011). In particular, there is a strong correlation between R&D investments and the number of patents (Griliches, 1998). In order to determine the developmental prospects in the field of biotechnology of rapeseed, the databases of the German Patent Office (DEPATISnet), the Polish Patent Office (PPO), and the European Patent Office (EPO—Espacenet) were examined in this study. The numbers of patent publications regarding rapeseed year by year were examined and compared. The data relating to patents were collected based on International Patent Classification (IPC, 2019.01 version)[1] codes and keywords.

Following the guidelines outlined in OECD (2005, 2008), a search encompassing the years between 1999 and 2017 was performed within the abovementioned databases. A presence of specific classification codes in a patent application (indicated by examiners of patent offices) means an affiliation with a specific industrial sector. **Table 1** shows the IPC classes, in which the number of inventions involving oilseed rape is represented most frequently. A full text search (i.e. including the title, abstracts, description and patent claims) was performed for each year of the date range. IPC classes typical for the area of biotechnology (OECD, 2008) were included in the results. Consequently, classes outside the area of biotechnology (e.g. machinery) were excluded from the search. To properly understand the meaning of the IPC codes indicated in a patent, it is necessary to know that one invention usually has several IPC codes, e.g., invention—a method of producing fat for chocolate products has an IPC code for the C07 class—organic chemistry and A23—food, in general.

The numbers of inventions involving rapeseed plants or their products were identified for each year. The term "involving rapeseed" means inventions concerning the plant itself, as well as products thereof, used for achieving inventions in any process. Therefore, a broad spectrum of rapeseed applications was included in the research study. The patent data analysis does not distinguish between domestic and foreign applicants in a given patent office. For instance, the numbers obtained for the PPO include both Polish and foreign applicants. The term "Polish application" means an application filed with the PPO, "German application" means an application filed with the German Patent Office, etc. The study could render more precise results as to the specific uses of patented inventions, but this would require a detailed analysis of the contents of the thousands of identified patent documents and could not be carried out within the ramifications of this project.

Obtained data were gathered for each of the patent offices separately and plotted on the charts (**Figures 3–8**). Trends indicating prospects for development for each of the offices were calculated using least squares regression analysis carried out in the Statistica software.

TABLE 1 | Definitions and contents of the most relevant IPC classes.

IPC symbol	CONTENT
A01	agriculture, forestry, animal husbandry, hunting, trapping, fishing – soil working in agriculture or forestry – planting; sowing; fertilizing – harvesting – horticulture; cultivation of vegetables, flowers, rice, fruit, vines, hops, or seaweed; forestry; watering – new plants or processes for obtaining them; plant reproduction by tissue culture techniques – manufacture of dairy products – preservation of bodies of humans or animals or plants or parts thereof – biocides, e.g., as disinfectants, pesticides or herbicides – biocidal, pest repellant, pest attractant or plant growth regulatory activity of chemical compounds or preparations
A21	baking, for making or processing doughs, doughs for baking – handling baked articles made from dough – treatment, e.g., preservation of flour or dough for baking, e.g. by addition of materials; baking; bakery products; preservation thereof
A23	foods or foodstuffs – preserving, e.g., by canning, meat, fish, eggs, fruit, vegetables, edible seeds; chemical ripening of fruit or vegetables; the preserved, ripened, or canned products – dairy products, e.g., milk, butter, cheese; milk or cheese substitutes; making thereof – edible oils or fats, e.g., margarines, shortenings, cooking oils – coffee; tea; their substitutes; manufacture, preparation, or infusion thereof – protein compositions for foodstuffs; working-up proteins for foodstuffs – feeding stuffs specially adapted for animals; methods specially adapted for production thereof – foods, foodstuffs, or non-alcoholic beverages – preservation of foods or foodstuffs
A61	medical or veterinary science; hygiene – preparations for medical, dental, or toilet purposes – specific therapeutic activity of chemical compounds or medicinal preparations
C07	organic chemistry – general methods of organic chemistry – organic compounds
C08	organic macromolecular compounds; their preparation or chemical working-up; compositions based thereon
C09	dyes, paints; polishes; natural resins; adhesives; compositions not otherwise provided for; applications of materials not otherwise provided for
C10	petroleum, gas or coke industries; technical gases containing carbon monoxide; fuels; lubricants; peat
C11	animal or vegetable oils, fats, fatty substances or waxes; fatty acids therefrom; detergents; candles
C12	biochemistry, beer; spirits; wine; vinegar; microbiology; enzymology; mutation or genetic engineering

Source: based on WIPO classification (2019).

The sample of plant variety rights analyzed in this paper was derived from the Community Plant Variety Rights Office (CPVO) database. The search encompasses plant variety rights

[1]The IPC (established by the Strasbourg Agreement, 1971) provides a stratified system of language independent symbols for the classification of patents and utility models in line with the different areas of technology to which they pertain (see World Intellectual Property Organization - WIPO classification).

granted for rapeseed between 1995 (the creation of the database) and 2018 (last full year of the study). Initially, 788 plant variety rights for rapeseed were identified within the examined period. Those were consequently matched with the year in which they were granted.

Standard least squares regression analysis was carried out for the gathered data set in order to plot the trend line within the analyzed period. The sample was also filtered by the nationality of subjects to whom rights were granted, in order to see the scope of innovative activity and the willingness to protect its effects in Poland and Germany, respectively. A company was treated as a company based in a particular country if its main seat is based in said country. Hence, the number of rights granted to, e.g., a German company, includes those granted to its subsidiaries in other countries. Conversely, rights granted to a German branch of a company based in a different country were rejected.

RESULTS AND DISCUSSION

Economic Aspects of Rapeseed Cultivation in the EU

According to the data from DG AGRI in the EU in 2017, the production of oilseeds (rapeseed, sunflower seed, soybean, linseed) amounted to 35 million tons, with rapeseed accounting for 22 million tons (63% of oilseeds). EU was the largest rapeseed producer (approximately 30% of world production) (FAOSTAT, 2018). The highest rapeseed production, 24 million tons, was in 2014 (see **Figure 1**).

The forecasted production (f) of oilseeds in 2019 is lower by approximately 2.2 million tons than in 2017 (**Figure 1**). However, according to the data (DG AGRI, 2019) the production of rapeseed is anticipated to increase by 18 000 tons in 2019.

The production of rapeseed in Poland in 2017 amounted to 2.7 million tons, whereas production in Germany amounted to 4.3 million tons (**Figure 2**). The volume of rapeseed production changed significantly from 2008 to 2017. The production of rapeseed in Germany is higher than in Poland; however, differences between the countries are decreasing year by year. Rapeseed can be the fastest developing crop in Poland, mainly because of its use in biodiesel production. However, data for the last decade show a slight decrease in the use of rapeseed as a source of biodiesel (USDA EU-28, 2019) concurrently with an increase in the overall use of biodiesel. Biodiesel is the most important among many types of biofuels produced and used in the EU (Sorda et al., 2010). Spain, Germany, and France lead among EU countries in biodiesel production (Eurostat, 2019). According to Eurostat (2019), in 2016, biodiesel production in EU countries reached approximately 21 million tons. In Poland, the production of biodiesels accounted for 1.15 million tons, whereas in Germany, it was 4.1 million tons.

In 2017, in EU countries, the area of rapeseed accounted for 6.7 million hectares (**Table 2**). In Poland, it was 0.91 million hectares (14% of the area of rapeseed in EU), whereas, in Germany, it was 1.3 million hectares (19.4% of the area). Due to dry sowing conditions in some major rapeseed producing countries, rapeseed acreage has declined sharply, especially in France and Germany (USDA EU-28, 2019). The area of rapeseed cultivation in Poland and Germany was characterized by frequent changes resulting from decrease of planting and unfavorable weather conditions. In Poland, a 19% increase in cultivated area was observed in 2017 compared to 2008. In Germany in 2017, the area of cultivation for this plant was decreased. Nevertheless, when looking from a longer time perspective, one can observe a steady upward trend in Poland since the 1950s combined with a sudden increase in the decade between 2005 and 2015 (from 0.55 million to 0.95 million hectares) and a plateau in recent years (CSO, 2018). This finding may indicate that, for now, the demand for rapeseed has stabilized.

EU imported 3.6 million tons of rapeseed in 2013–2017, mainly from Australia (44%) and Ukraine (36%). It is worth to mention that in 2018–2019, import of rapeseed increased to 4.2 million tons (EU Oilseed Complex, 2019). A significant

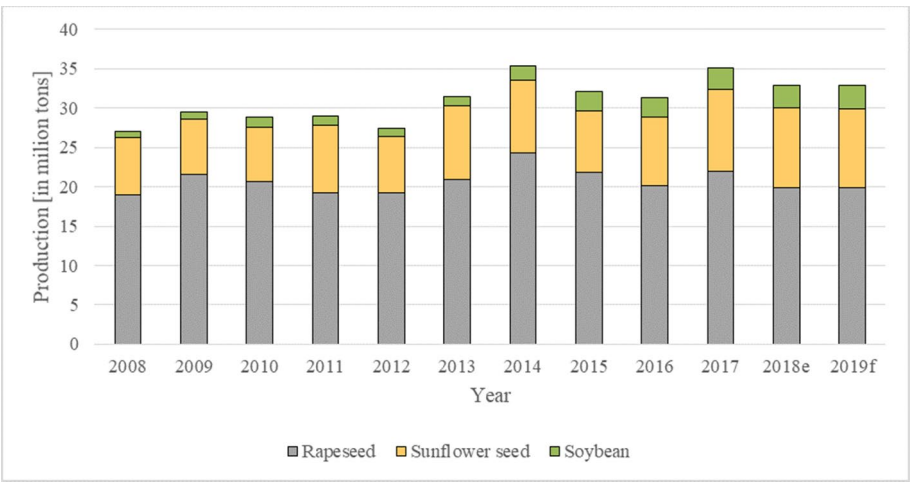

FIGURE 1 | Production of oilseeds in EU 2008–2019, (f – forecasted production; e – estimated production). Source: own study based on data from DG AGRI and Eurostat 2019.

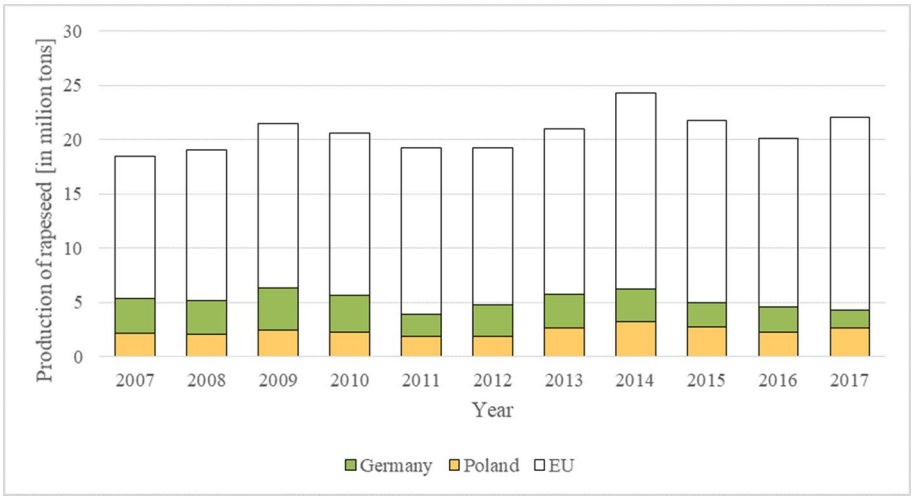

FIGURE 2 | Production of rapeseed in Germany and Poland from 2008 to 2017. Source: own study based on data from DG AGRI and Eurostat 2019.

TABLE 2 | The area of rapeseed cultivation in the EU, Germany, and Poland in millions of hectares.

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
EU-28	6.1736	6.5307	7.1056	6.7483	6.2091	6.7136	6.7144	6.4672	6.5347	6.7488
Germany	1.3707	1.4712	1.4612	1.3286	1.3062	1.4656	1.3942	1.2855	1.3257	1.3089
Poland	0.7711	0.8100	0.9461	0.8301	0.7203	0.9207	0.9511	0.9471	0.8226	0.9143

Source: own study based on data from DG AGRI and Eurostat 2019.

share of the EU oilseed plants import belongs to GM soybean. According to the EU Commission, between 2014 and 2016, the EU imported more than 30 million tons of GM soybean annually, including Poland, which imported 2 million tons (Rostoks et al., 2019). Replacing imported GM soybean meal with domestically grown oilseed, such as rapeseed, in the feed industry is currently not an achievable and practical alternative because of technical and climatic limitations.

Patents and Plant Variety Rights—Analysis and Comparisons

European Patents

The number of European patent publications was characterized by a steady increase between 1999 and 2017 (**Figure 3**). A look at different IPC classes, where none are dominating (**Figure 4**), shows a widespread research and use of rapeseed in different areas and may be seen as reflecting its industrial potential in

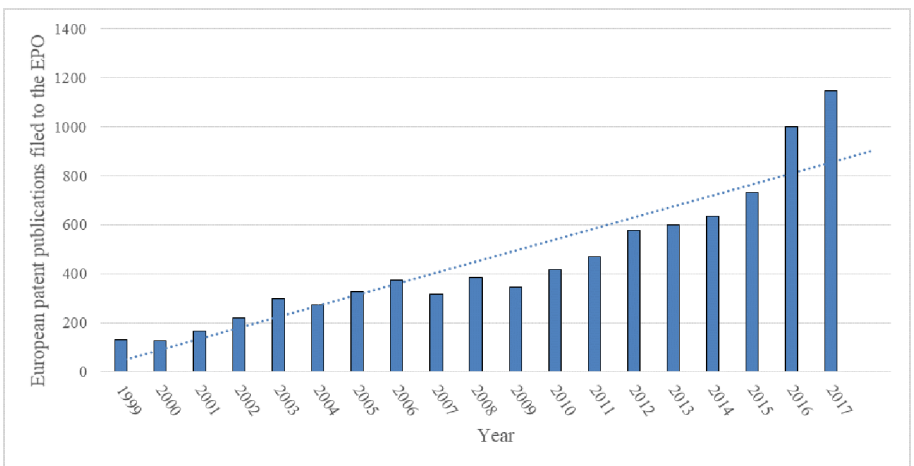

FIGURE 3 | Number of European patent publications filed to the EPO from 1999 to 2017 that use rapeseed or any product thereof and their trend (full text search). Source: own study based on data from Espacenet.

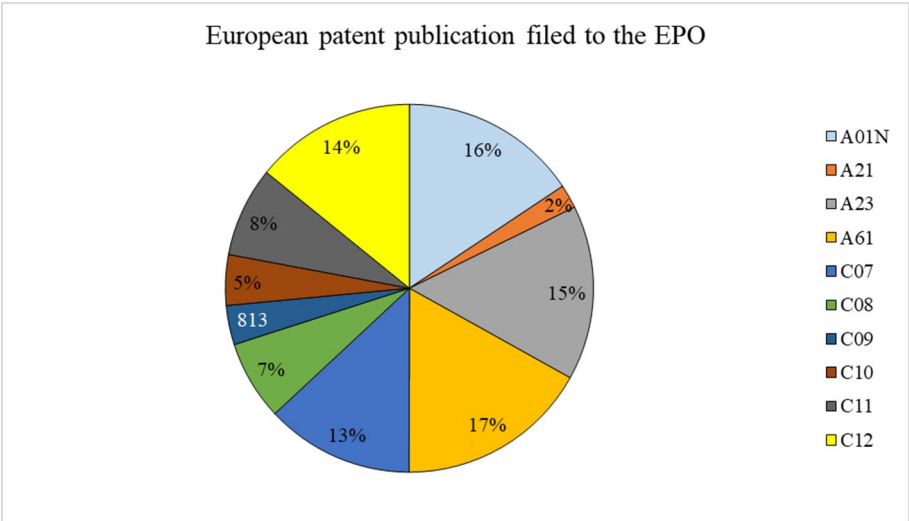

FIGURE 4 | European patent publications (in %) filed to the EPO from 1999 to 2017 that use rapeseed itself or any product thereof in different industrial fields (full text search). See **Table 1** for the explanation of the symbols. Source: own study based on data from Espacenet.

agriculture, i.e., soil working, planting, harvesting, cultivating vegetables, developing new plants or the processes for obtaining them, and manufacturing dairy products, as well as in biocides, e.g., disinfectants, pesticides or herbicides, or plant growth regulators.

The numbers of patent publications per year are an order or in some years two orders of magnitude higher than for either of the national offices examined. This does not necessarily indicate the level of R&D investments in respective countries, but rather the popularity of each of the examined offices. A European patent can provide protection in multiple European countries, including Germany and Poland. Unlike in the case of the national offices, what stands out in the presented chart (**Figure 3**) is a continual growth of the number of patent publications each year. This in turn, coupled with the abovementioned correlation between patent data and the R&D investment levels can indicate R&D investments in rapeseed and rapeseed connected technologies. Since patents are granted for inventions that have to show improvements in comparison to previously patented ones, a growing trend indicates an acceleration of development of a given area year to year (even a horizontal trend line in this case would mean that new solutions are being developed each year and as such would show progress, not stagnation).

Polish Patents

The data on Polish patents show a frequent year to year changes with almost a horizontal trend line (**Figure 5**). The highest number of patents granted in the PPO are applications in the IPC

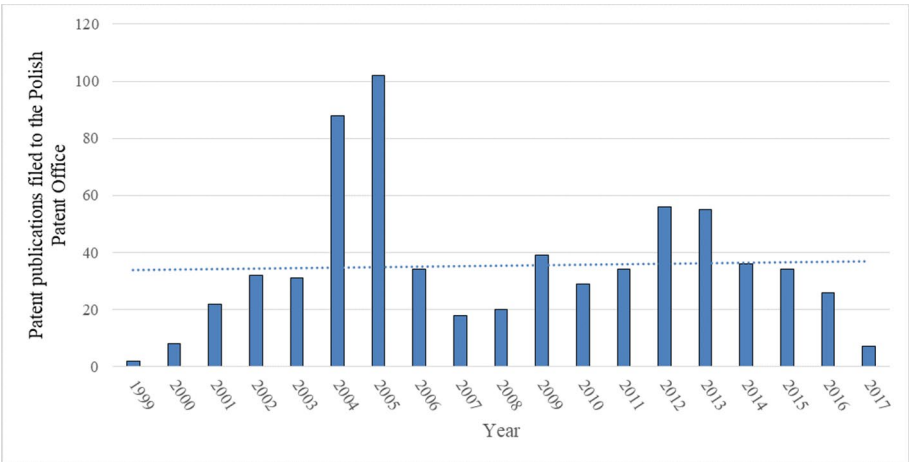

FIGURE 5 | Number of patent publications filed to the Polish Patent Office from 1999 to 2017 regarding inventions that use rapeseed or any product thereof, and their trend (full text search). Source: own study based on data from the Polish Patent Office (2018).

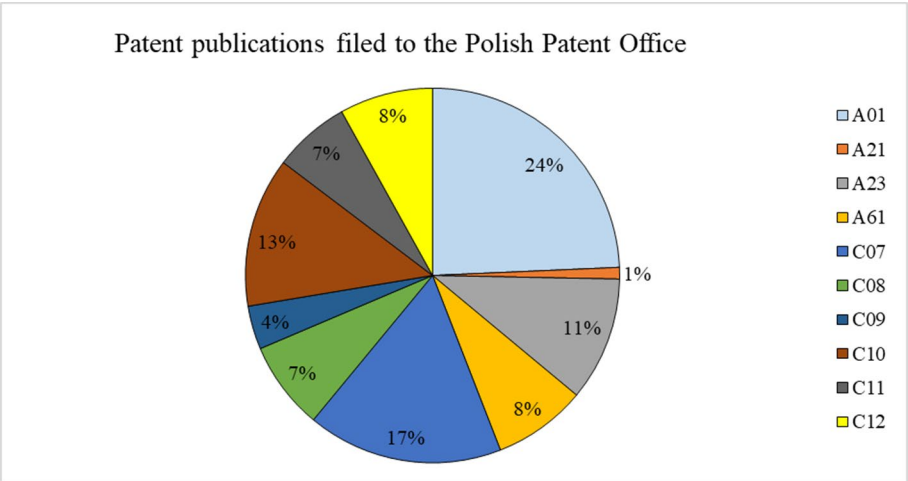

FIGURE 6 | Polish patents (in %) filed to the Polish Patent Office from 1999 to 2017 that use rapeseed itself or any product thereof in different industrial fields (full text search). See **Table 1** for the explanation of the symbols. Source: own study based on data from the Polish Patent Office (2018).

class A01—24% (**Figure 6**). It was to be expected, as this is the broadest class covering agriculture, forestry, animal husbandry, hunting, trapping, and fishing. Organic chemistry (class C07) is the second most common application—17% (**Figure 6**). It is important to note that, in Poland, many inventions (13%) cover the use of rapeseed in the petroleum or gas industries (IPC-C10). The number of Polish patents for genetically modified (GM) rapeseed itself or involving any products thereof in genetic engineering was 22 from 1999 to 2017 (C12N15/82 of IPC).

German Patents

The number of patent publications changed in the period from 1999 to 2006 and remained at a high level (**Figure 7**). The number of patent publications in Germany was characterized by frequent changes. After 2007, the number of patent publications of the German Patent Office decreased. There are clearly marked years of stable growth (1999–2007) and years of decline (2008–2017). This observation should be analyzed in detail in the future.

The largest proportion of patent publications filed in the German Patent Office came from agriculture (38%), organic chemistry (20%), and biochemistry (11%) (**Figure 8**). The number of German patent applications regarding GM rapeseed itself or involving any products thereof in genetic engineering was 186 between 1999 and 2017 (C12N15/82 of IPC).

Plant Variety Rights

Plant variety rights and patents exist simultaneously in Europe, sometimes protecting the same solutions. Although the

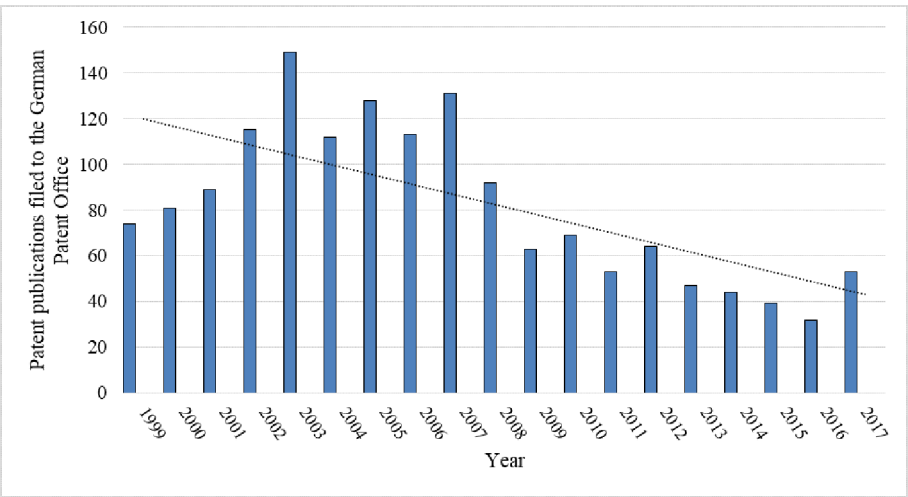

FIGURE 7 | Number of patent publications filed to the German Patent Office from 1999 to 2017 regarding inventions that use rapeseed or any product thereof and their trend (full text search). Source: own study based on data from DEPATISnet (2019).

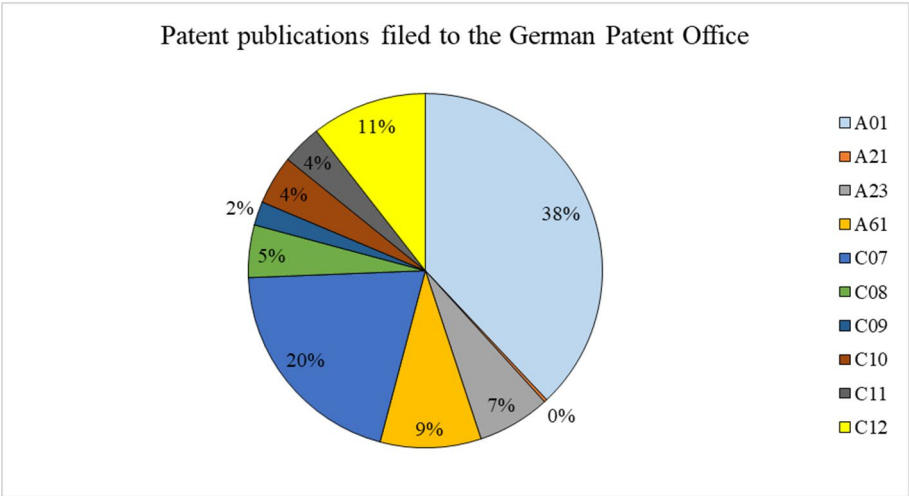

FIGURE 8 | Patent publications (in %) filed to the German Patent Office from 1999 to 2017 that use rapeseed itself or any product thereof in different industrial fields (full text search). See **Table 1** for the explanation of the symbols. Source: own study based on data from DEPATISnet (2019).

European Patent Convention (EPC) outright forbids granting of patents for plant varieties (art. 53b), it does not preclude granting patents to groupings broader than a variety, even if such a group encompasses varieties (see EPO, 2018a; EPO, 2018b. Guidelines for Examination to the EPO part G.II.5.4.1). Hence, a patented invention can find its application within multiple protected varieties.

Steady progress in the breeding of rapeseed can be observed in the last decade, with the number of plant variety rights granted for new rapeseed varieties growing and clearly exceeding the numbers from before 2010 (**Figure 9**).

In the area of plant variety rights, a domination of large companies can be shown, with seven companies owning over 80% of the rights (see **Table 3**). Out of all the rights granted from 2000 to 2018, over half (396) belonged to German companies and only 2 to Polish companies. The numbers for the years 2017–2018 may not fully represent the number of rights granted, due to a delay in the delivery of decisions. As of May 2019, there were still 6 applications active for 2017 and 32 for 2018. The number of active applications filed already in 2019 was 48.

The data on plant variety rights show that the level of innovativeness in breeding is currently higher than that in

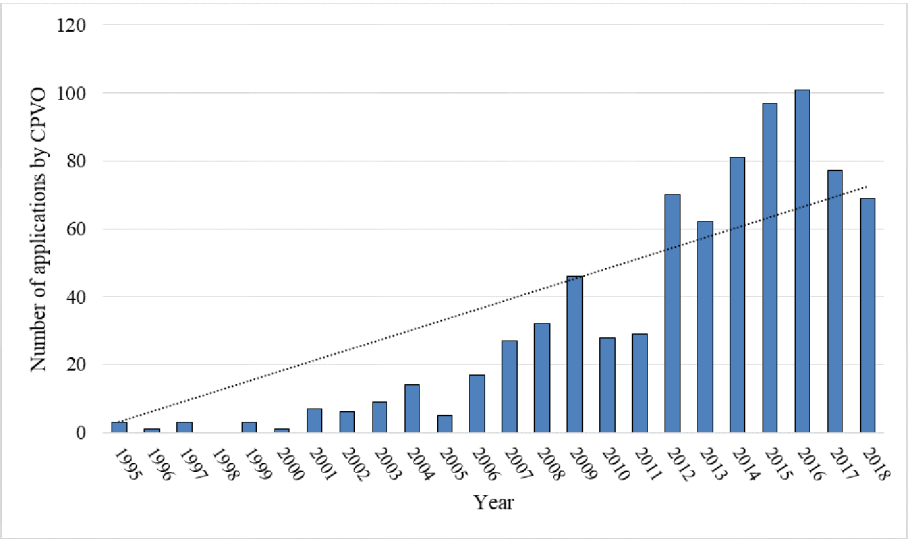

FIGURE 9 | Number of applications for which exclusive plant variety rights were granted 1995–2018 and their trend. Source: own study based on data from CPVO (2019).

TABLE 3 | Companies to whom plant variety rights were granted.

Company	Number of rights
KWS	191
Monsanto	95
Pioneer	95
Norddeutsche Pflanzenzucht	93
Deutsche Saatveredelung	69
Syngenta	56
Limagrain	41
BASF	29
Euralis	29
Lantmännen	24
RAGT	18
Caussade	16
Saatzucht Donau GmbH & Co. KG	10
JTSD	4
Selgen	4
Knold & Top	3
W. von Borries-Eckendorf GmbH & Co. KG	3
Saatbau Linz eGen	2
Lammers Seed Options	1
Maïsadour	1
Smolice	1
Strzelce	1

Source: based on CPVO (2019).

the previous decade and, like in the case of European patents, the pace of progress seems to be increasing. Despite rapeseed being a widespread crop in Poland, Polish breeding companies do not seem to apply for EU plant variety rights. This finding may indicate either a low level of innovativeness or the low attractiveness of the rights themselves. In comparison, the number of rights possessed by German companies is higher by two orders of magnitude. Despite having rapeseed production at a comparable level, the Polish farming industry does not seem to contribute to its biological progress as much as the German industry. There may be various reasons for this fact, including the low collectability of royalties in Poland or farmers' reluctance to grow newer varieties.

Legal Ramifications of Novel Methods of Breeding in the EU

No GM varieties of rapeseed are grown in the EU, since none were authorized for cultivation. In 2017, the share of GM rapeseed in the global area of biotech crops was 5% (50% of the area was occupied by GM soybean) (ISAAA, 2018). The global area of GM rapeseed increased by 19% from 8.6 million hectares in 2016 to 10.2 million hectares in 2017. This change occurred due to the adoption of new GM rapeseed varieties with nutritious oil content and different types of herbicide tolerant traits. Herbicide tolerant rapeseed is the fifth most important biotech plant trait commercialized since 1996; it has been adopted largely in Canada, the USA, and Australia (ISAAA, 2018). Moreover, the global area and adoption of rapeseed could increase significantly in the near term in response to the likely increased use of rapeseed for vegetable oil and biodiesel (ISAAA, 2018).

The use of GM products as food and feed in the EU is strongly limited due not only to the strictness of criteria but also to the length and uncertainty of the authorization process, which may work as a deterrent when choosing the breeding method (Zimny et al., 2019). A recent dispute regarding the legal status of products of certain new plant breeding techniques (NBTs) from the point of view of EU genetically modified organisms (GMOs) legislation may lead to legal uncertainty and may work as another deterrent when choosing such breeding methods as Site Directed Nucleases or Oligonucleotide Directed Mutagenesis. In a recent judgment in the case C-528/16, the Court of Justice of the European Union ruled that only organisms obtained by "means of techniques/methods of mutagenesis, which have conventionally been used in a number of applications and have a long safety record," are exempted from the scope of Directive 2001/18/EC on the deliberate release of GMOs to the environment (Directive, 2001). As noted by Smyth and Lassoued (2019), this judgment may have detrimental impacts on agricultural innovations, R&D funding, and international trade.

According to Eriksson et al. (2019a), it is a paradox related to GM food and feed that 62 different transformation events that have passed the risk assessment by the European Food Safety Authority (EFSA) are entering the EU as food and feed, but only one can be planted in the EU (the MON 810 maize). The authors described two scenarios for implementing a national opt-in mechanism for the cultivation of GM plants under EU legislation and highlighted that if member states have the right to opt out of GM crop cultivation, they should also have a right to opt in (Eriksson et al., 2019a).

The legal disputes regarding novel methods of plant breeding, including those applied to rapeseed, may hamper the development of technologies that would allow for the optimal use of rapeseed as a food and industrial crop and its future potential.

CONCLUSIONS

Analyzed data on patent numbers and plant variety rights show potential of rapeseed use in the food and feed industries, as well as in industrial applications (as follows from the analysis of the IPC classes). What clearly results from this work is that rapeseed is a popular crop in both compared countries—Poland and Germany. After a dynamic growth, the acreage of rapeseed cultivation has been rather steady over the last few years and subject to periodical fluctuations. While used mostly as a source of food and feed, rapeseed also has industrial applications. Its use as a substrate for the production of biodiesel has not only stagnated in recent years but also shows a slight decrease.

The continuation of the development of new varieties is required to expand rapeseed cultivation. As indicated previously the EU, Poland and Germany are not self-sufficient in terms of demand for protein feedstuffs and for energy; for this reason, EU imported more than 30 million tons of GM soybean. If imported GM soybean can be replaced by additional oilseeds grown in EU countries, it would require additional area.

Taking advantage of the full potential of rapeseed would require the utilization of whole plants, and such research is already being carried out. Nevertheless, a multi-faceted utilization of rapeseed products requires not only progress in processing technologies

but also in breeding (Campbell et al., 2016). It is through breeding that the genetic diversity of rapeseed could be increased so that it could be used as a sustainable product with multiple applications. Countries such as Poland and Germany are particularly suitable for making use of that potential. The comparison of the IPR management policies of those countries' breeders shows that Germany has a very significant advantage in this respect over Poland. Despite showing comparable demand for rapeseed, both countries differ significantly in regard to the protection of new varieties. It is difficult to explain this phenomenon without analyzing company policies, and such an examination was beyond the scope of the study and may also be hampered by a particular company's unwillingness to share such policies.

The seed market in EU is highly concentrated, and the majority of rights are held by several companies (a large proportion of them—German), who can show rather broad plant variety rights and patent portfolios. It seems then that these companies will likely indicate the directions for crop development in the foreseeable future. However, all breeders are currently limited in their choice of breeding methods with regard to the introduction of new products to the EU market. These limitations stem from a practical inability to introduce GM products for cultivation in the EU. Another obstacle is the legal uncertainty regarding the status of the products of NBTs, which may work as a deterring factor in choosing a breeding method, since treating its products as GMOs reguiring authorization effectively renders them unsuitable for the development of new varieties for the EU market. These factors may strongly contribute to the sub-optimal usage of rapeseed's potential, particularly in comparison to countries with clearer or more liberal policies towards NBTs. This uncertainty and legal obstacles are not encountered by entrepreneurs from other parts of the world (e. g. Argentina or the USA (Eriksson et al., 2019b) and might put European entrepreneurs at a competitive disadvantage.

The analysis of exclusive rights granted for rapeseed-connected inventions and rapeseed varieties shows that there is a growing trend in regard to the numbers of those rights granted. This trend may indicate prospects for the development of the analyzed crop and possibly – its new applications. The growing trend in the number of patent applications can be observed in the case of applications filed with the EPO (counted in thousands), while data from the national patent offices (applications counted in tens or hundreds) show the opposite phenomenon. This fact is rather a symptom of the dwindling popularity of national offices than of the lack of development of rapeseed itself. Trends in the numbers of plant variety rights granted seem concurrent with those of patent applications filed with EPO, showing a significant increase in the last decade. The data on European patents and plant variety rights seem to support the assumed hypothesis that rapeseed has potential to be further developed as a versatile, multi-use crop.

AUTHOR CONTRIBUTIONS

EWo and TT drafted the manuscript. EWo conducted the analysis and interpretation of the data related to economic aspects of rapeseed. EWa was responsible for obtaining and interpreting the patent data. TZ and SS presented a chapter on plant variety rights and took part in interpreting patent data. TT studied the conception and design and conducted critical revisions. All the authors reviewed and approved the final manuscript.

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REFERENCES

Andrews, D., and Criscuolo, C. (2013). Knowledge-Based Capital, Innovation and Resource Allocation. OECD Economics Department Working Papers, No. 1046. Paris: OECD Publishing. doi: 10.1787/5k46bj546kzs-en (Accessed June 15, 2019).

Brzóska, F., Śliwiński, B., and Michalik-Rutkowska, O. (2010). Pasze rzepakowe – miejsce w bilansie białkowym kraju oraz wartość pokarmowa. *Cz. 1. Wiad. Zootech.* 48, 11–18.

Campbell, L., Rempel, C. B., and Wanasundara, J. P. (2016). Canola/Rapeseed protein: future opportunities and directions-workshop proceedings of IRC 2015. *Plants (Basel)* 5, E17. doi: 10.3390/plants5020017

Canola Council (2017). What is canola. Available at: https://www.canolacouncil.org/oil-and-meal/what-is-canola/ (Accessed May 12, 2019).

Coad, A., and Rao, R. (2006). Innovation and market value: a quantile regression analysis. *Econ. Bull.* 15, 1–10.

Community Plant Variety Office - CPVO (2019). Public search. Available at: https://cpvoextranet.cpvo.europa.eu/mypvr/#!/en/publicsearch (Accessed May 23, 2019).

CSO - Statistics Poland (2018). *Statistical Yearbook of Agriculture in 2017 in Poland*. Warsaw, Poland: CSO.

Directive (2001) EC of the European Parliament and od the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing. Council Directive 90/220/EEC.

Directorate-General for Agriculture and Rural Development - DG AGRI (2019). Agriculture in the European Union and the Member States - Statistical factsheets. Available at: https://ec.europa.eu/agriculture/statistics_en (Accessed April 01, 2019).

Dubarić, E., Giannoccaro, D., Bengtsson, R., and Ackermann, T. (2011). Patent data as indicators of wind power technology development. *World Pat. Inf.* 33, 144–149. doi: 10.1016/j.wpi.2010.12.005

Eriksson, D., de Andrade, E., Bohanec, B., Chatzopoulou, S., Defez, R., Leiva Eriksson, N., et al (2019a). Implementing an EU opt-in mechanism for GM crop cultivation. *EMBO Rep.* 20, e48036. doi: 10.15252/embr.201948036

Eriksson, D., Kershen, D., Nepomuceno, A., Pogson, B. J., Prieto, H., Purnhagen, K., et al (2019b). A comparison of the EU regulatory approach to directed mutagenesis with that of other jurisdictions, consequences for international

trade and potential steps forward. *New Phytol.* 222, 1673–1684. doi: 10.1111/nph.15627

EU Oilseed Complex (2019). Oilseed Complex Trade. Available at: https://circabc.europa.eu/sd/a/ecca07a5-5d56-47b1-a678-e24cceeb450c/oilseeds-trade-2017-18-marketing-year-July-December.pdf (Accessed September 10, 2019).

European Commission (2013). *PATLICE Survey - Survey on Patent Licensing Activities by Patenting Firms*. Vienna: Technopolis Group.

European Patent Office (2018). ESPACENET database. Available at: https://worldwide.espacenet.com/ (Accessed April 10, 2019).

European Patent Office (2018). Guidelines for Examination to the European Patent Office, Munich: EPO.

Eurostat (2019). Database: Infrastructure - biofuel production capacities - annual data. Available at: https://www.ec.europa.eu (Accessed 12 May, 2019).

Food and Agriculture Organization of the United Nations - FAOSTAT (2018). Database - crops production. Available at: https://www.fao.org/faostat/en/#data/QC (Accessed May 12, 2019).

German Patent Office DEPATISnet (2019). Database. Available at: https://www.dpma.de/patente/index.html (Accessed April 10, 2019).

Griliches, Z. (1998). "Patent Statistics as Economic Indicators: A Survey," in *R & D and productivity: the econometric evidence A National Bureau of Economic Research monograph* (Chicago: Univ. of Chicago Press), 287–343. Available at: http://www.nber.org/chapters/c8351 [Accessed September 10, 2019].

Herkes, J. (2019). Rapeseed and canola for biodiesel production. Available at: https://farm-energy.extension.org/rapeseed-and-canola-for-biodiesel-production/ (Accessed May 12, 2019).

Institute of Agricultural and Food Economics - National Research Institute in Poland (2018). Market analysis. Available at: https://www.ierigz.waw.pl (Accessed May 02, 2019).

ISAAA (2018). Global Status of Commercialized Biotech/GM Crops in 2017: Biotech Crop Adoption Surges as Economic Benefits Accumulate in 22 years. ISAAA Brief No. 53. Ithaca, NY: ISAAA.

Kaczmarek, P., Korniewicz, D., Lipiński, K., and Mazur-Kuśnirek, M. (2016). Chemical composition of rapeseed products and their use in pig nutrition. *Pol. J. Nat. Sci.* 31, 545–562.

Kdidi, S., Vaca-Medina, G., Peydecastaing, J., Oukarroum, A., Fayoud, N., and Barakat, A. (2019). Electrostatic separation for sustainable production of rapeseed oil cake protein concentrate: effect of mechanical disruption on protein and lignocellulosic fiber separation. *Powder Technol.* 344, 10–16. doi: 10.1016/j.powtec.2018.11.107

Main Inspector of Plant Health and Seed Inspection in Poland (2018). Seed material. Available at: https://piorin.gov.pl/nasiennictwo/ocena-materialu-siewnego/ (Accessed May 15, 2019).

Negahdar, L., Gonzalez-Quiroga, A., Otyuskaya, D., Toraman, H. E., Liu, L., Jastrzebski, J. T., et al (2016). Characterization and comparison of fast pyrolysis bio-oils from pinewood, rapeseed cake, and wheat straw using (13)C NMR and comprehensive GC x GC. *ACS Sustain. Chem. Eng.* 4, 4974–4985. doi: 10.1021/acssuschemeng.6b01329

OECD (2005). A Framework for Biotechnology Statistics. OECD Available at: http://www.oecd.org/sti/sci-tech/34935605.pdf [Accessed March 3, 2019].

OECD (2008). OECD Patent Databases. Identifying Technology Areas for Patents. Available at: http://www.oecd.org/sti/inno/40807441.pdf [Accessed March 7, 2019].

OECD-FAO (2018). FAO agricultural outlook. Available at: https://stats.oecd.org/ (Accessed April 03, 2019).

Ogrodowczyk, M., and Bartkowiak-Broda, I. (2013). Ocena postępu biologicznego w hodowli rzepaku (*Brassica napus* L.). *Rośl Oleiste – Oilseed Crops* 34, 289–301.

Pilkington, A., Dyerson, R., and Tissier, O. (2002). The electric vehicle:: Patent data as indicators of technological development. *World Pat. Inf.* 24, 5–12. doi: 10.1016/S0172-2190(01)00065-5

Polish Patent Office (2018). Quick search. Available at: https://www.uprp.pl/ (Accessed April 20, 2019).

Rostoks, N., Grantina-Ievina, L., Levina, B., Evelone, V., Valcina, O., Aleksejeva, I. (2019). Genetically modified seeds and plant propagating material in Europe: potential routes of entrance and current status. *Heliyon* 5 (2), e01242. doi: 10.1016/j.heliyon.2019.e01242.

Smyth, S. J., and Lassoued, R. (2019). Agriculture R&D implications of the CJEU's gene-specific mutagenesis ruling. *Trends Biotechnol.* 37, 337–340. doi: 10.1016/j.tibtech.2018.09.004

Sorda, G., Banse, M., and Kemfert, C. (2010). An overview of biofuel policies across the world. *Energy Policy* 38, 6977–6988. doi: 10.1016/j.enpol.2010.06.066

USDA EU-28 (2019). Oilseeds and products annual. Available at: https://www.fas.usda.gov/data/eu-28-oilseeds-and-products-annual-3 (Accessed April 10, 2019).

Wang, Z.-W., Zhu, M.-Q., Li, M.-F., Wei, Q., and Sun, R.-C. (2019). Effects of hydrothermal treatment on enhancing enzymatic hydrolysis of rapeseed straw. Renew. *Energy* 134, 446–452. doi: 10.1016/j.renene.2018.11.019

WIPO classification (2019). World intellectual property organization database. Available at: https://www.wipo.int/classifications/ipc/en/ (Accessed April 15, 2019).

Woźniak, E., and Twardowski, T. (2018). GMO – is it possible to breed livestock without GM feed in Poland? *Nauka* 3, 155–173.

Zimny, T., Sowa, S., Tyczewska, A., and Twardowski, T. (2019). Certain new plant breeding techniques and their marketability in the context of EU GMO legislation - recent developments. *N. Biotechnol.* 51, 49–56. doi: 10.1016/j.nbt.2019.02.003

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frontiers in Plant Science

REVIEW
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Induced Genetic Variation in Crop Plants by Random or Targeted Mutagenesis: Convergence and Differences

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New Breeding Techniques (NBTs) include several new technologies for introduction of new variation into crop plants for plant breeding, in particular the methods that aim to make targeted mutagenesis at specific sites in the plant genome (NBT mutagenesis). However, following that the French highest legislative body for administrative justice, the Conseil d'État, has sought advice from The Court of Justice of the European Union (CJEU) in interpreting the scope of the genetically modified organisms (GMO) Directive, CJEU in a decision from 2018, stated that organisms modified by these new techniques are not exempted from the current EU GMO legislation. The decision was based in a context of conventional plant breeding using mutagenesis of crop plants by physical or chemical treatments. These plants are explicitly exempted from the EU GMO legislation, based on the long-termed use of mutagenesis. Following its decision, the EU Court considers that the NBTs operate "at a rate out of all proportion to those resulting from the application of conventional methods of mutagenesis." In this paper, we argue that in fact this is not the case anymore; instead, a convergence has taken place between conventional mutagenesis and NBTs, in particular due to the possibilities of TILLING methods that allow the fast detection of mutations in any gene of a genome. Thus, by both strategies mutations in any gene across the genome can be obtained at a rather high speed. However, the differences between the strategies are 1) the precision of the exact site of mutation in a target gene, and 2) the number of off-target mutations affecting other genes than the target gene. Both aspects favour the NBT methods, which provide more precision and fewer off-target mutations. This is in stark contrast to the different status of the two technologies with respect to EU GMO legislation. In the future, this situation is not sustainable for the European plant breeding industry, since it is expected that restrictions on the use of NBTs will be weaker outside Europe. This calls for reconsiderations of the EU legislation of plants generated *via* NBT mutagenesis.

Keywords: conventional mutagenesis, EU legislation, New Breeding Techniques (NBT), NBT mutagenesis, precision breeding, off-target mutations

INTRODUCTION

Plant breeding is a discipline for targeted and continuous development of new plant varieties. It utilizes the genetic variation between individuals within a plant species and combines the desired properties into new and improved varieties. Plant breeding is dependent on genetic variation, and new variation is fundamentally important for introduction of new traits in breeding programs. However, in cases where a specific genetic trait is not immediately available to be crossed into breeding materials, the genetic variation in a crop species can be expanded by other means. For decades this has been achieved by, e.g., chemical or physical treatments, translocation breeding, synthetic hexaploids, etc; techniques that involve comprehensive changes of the plant's genome. Due to its long safety record, organisms obtained by physical and chemical mutagenesis are exempt from the provisions of the GMO legislation in the EU. Nevertheless, the methods incite hundreds or even thousands of random mutations with unknown effects and consequences.

New Breeding Techniques (NBT) include several new technologies for introduction of variation into crop plants. NBT comprises a number of technologies that have emerged since the current Directive 2001/18/EC on GM plants was implemented. At the request of the member states, the European Commission set up a working group in 2007 to assess whether or not a number of new breeding techniques should fall within the scope of GMO legislation. The working group prepared a list of seven new plant breeding techniques: zinc finger nuclease (ZFN) technology, oligonucleotide-directed mutagenesis (ODM), cisgenesis and intragenesis, grafting on GM-rootstock, RNA-dependent DNAmethylation, agro-infiltration "sensu stricto," and reverse breeding. The ZFN technique is a site-directed nuclease (SDN) tool that can be designed to produce a mutation at a predetermined position in the plant genome. Since 2007, a number of new SDN tools have emerged, such as the TALEN and CRISPR/Cas techniques, of which, in particular, the latter is now widely used. It is beyond the scope of this paper to describe all the different NBTs in detail. Here we will focus on the two techniques involved in the generation of mutations at pre-determined sites in a plant genome, i.e., ODM and especially the SDN-tools. We will refer to these as NBT mutations and use the term precision breeding to describe the use of NBT mutations in plant breeding. The other NBTs are described in detail in (Lusser et al., 2012) and (Schaart et al., 2016). Common to almost all these techniques are, however, that the final plants, which are exposed to the open environment, are without foreign DNA as the vector constructs are either never integrated into the plant genome or are out-segregated in the next generation. Exceptions are cisgenesis/intragenesis, and the use of the SDN-tools to insert longer DNA fragments into pre-selected sites in the plant genome. Both of these techniques require that the transferred DNA is permanently integrated into the plant genome.

Early after their emergence, the SDN technologies were adopted to improve mutations already available from traditional mutagenesis. For example, in order to improve the quality of soy oil and avoid non-ideal mutations induced by traditional mutation, two target genes FAD2-1A and FAD2-1B were simultaneously mutated using TALENs (Haun et al., 2014). Functional mutations down to the deletion of two nucleotides were identified. In contrast, traditional induced mutations of FAD2-1A by x-ray are up to 164-kb deletions that may remove other desirable genes in addition to FAD2-1A (Bolon et al., 2011). In another early example, fragrant rice was generated by a SDN directed toward 1-bp deletion in the gene encoding betaine aldehyde dehydrogenase (BADH2). Traditionally induced mutations in the gene mutation are up to 803-bp deletions plus a range of unknown side mutations (Shan et al., 2015). Placed in the context of traditional mutagenesis methodologies in crops, the examples demonstrate how SDN technology improves precision and reduces the extent of mutations in a crop where a specific trait is pursued.

Only a few crops have been improved through the use of ODM, whereas the SDN tools are widely used. Without doubt, NBT mutations represents a significant progress for the breeding of crops for a challenging future. Speed and precision are often mentioned as key beneficial properties of the NBT mutations. However, on July 25, 2018, The Court of Justice of the European Union (CJEU) ruled that organisms obtained by these new mutagenesis technologies are not exempted from the current EU GMO legislation. (Court-of-Justice-of-the-European-Union, 2018) In order for precision bred crops to be exempted, the GMO Directive needs to be revised to reflect scientific progress in biotechnology. In the discussion of this, parallels must be drawn to the use of conventional mutation breeding as a way of inducing genetic variation in breeding material. Hence, it is worthwhile as a first step to look more closely into this approach; how it has been used and developed in plant breeding; and how it compares to the new targeted genome editing techniques, in particular the CRISPR/Cas9-based techniques. What are the differences and are there significant convergence between the old methods exempted from GM legislation and NBT mutations. In order to place NBT mutations in the context of today's breeding, we will in the current paper uncover major similarities and differences between NBT mutations and mutations obtained by conventional mutagenesis with respect to precision and off-target mutations.

Conventional Mutation Breeding in the Context of New Breeding Technologies

Mutation breeding has been used by plant breeders world-wide since the discovery in the 1920s that heritable mutations could be induced in plants by means of irradiation or chemical treatments (Stadler, 1928). The expectations to this method for improvements of crop varieties were big in the 1950s to 1960s, and indeed a considerable number of varieties was released, e.g. from Scandinavian barley breeding (Lundqvist, 2014). The mutated genes from these old mutant varieties are still part of the gene pool used for modern barley breeding. Since the 1980s, the interest among plant breeders in using mutation breeding has declined, probably due to expectations to the new genetic modification technologies (GM traits), but also due to difficulties in dealing with the load of accompanying bad mutations in selected lines, which hampered development of high-yielding varieties based on mutations (Mba, 2013). Nevertheless, even with

the harsh treatments of plants in the mutation breeding process aimed to induce genetic modifications, the plants coming out of it were explicitly exempted from the EU GMO legislation on GM crops, implemented almost 30 years ago (Directive 90/220/EEC and Directive 2001/18/EC), due to their long safety record.

Irradiation and treatment with chemical mutagens are the two major methods used to induce mutations in plants (Leitao, 2011; Mba et al., 2011). X-rays and gamma radiation cause a mixture of bigger chromosome deletions and point mutations, i.e., single base substitutions or deletions, whereas the most commonly used chemical mutagens (e.g. NaN_3, EMS, MNU) almost exclusively cause single base substitutions (transitive, i.e. from G/C to A/T; see **Table 1**). The advantage of the chemical mutagens is that they can be used to prepare mutant populations with high densities of mutations, making it easier to screen for specific mutations in a population (Szarejko et al., 2017).

By the turn of the century, a big change with respect to utilization of mutants took place following development of efficient TILLING (Targeting Induced Local Lesions in Genomes) techniques (Mccallum et al., 2000). Previously, mutation breeding was exclusively based on forward genetics, i.e. on phenotype screening for favorable traits in mutant populations. TILLING made reverse genetics approaches applicable, since this technique is aimed at the detection of mutations in specific, known genes. The use of TILLING has accompanied the general development of molecular insight into the genetic base for crop traits and development of efficient new generation DNA sequencing techniques. In principle, this now makes it possible to find mutations in any pre-selected gene across the genome of crop plants, if the DNA sequence of the gene is known and if a suitable mutant population is available (Jankowicz-Cieslak et al., 2017).

For the major European crops, barley and wheat, good TILLING population resources are already existing (Krasileva et al., 2017; Szurman-Zubrzycka et al., 2018), and for most seed propagated species TILLING populations can in principle be generated, if not available. In addition, new generation sequencing techniques (Burkart-Waco et al., 2017; Krasileva et al., 2017) and efficient methods to detect DNA heteroduplexes (Szurman-Zubrzycka et al., 2017) have made it easier than previously to screen the populations for mutations in selected target genes. Since the alkylating chemical mutagens mainly cause transitions in the chromosomal DNA, specific mutations can to a certain degree be predicted and searched for during screening of a mutant population. Hence, mutagenesis is not just a random tool to discover mutations, but can be partially directed. Furthermore, DNA marker-assisted backcrossing can make the transfer of mutations into elite varieties much more efficient than previously (Hasan et al., 2015).

Overall, the development of TILLING, stable mutant populations, and efficient backcrossing in principle now makes the acquisition of mutations in specific genes very efficient and fast for seed propagated crop species. This contrasts with the statement that were made by the CJEU in its 2018 decision on NBTs, namely that the new breeding "techniques make it possible to produce genetically modified varieties at a rate out of all proportion to those resulting from the application of conventional methods of mutagenesis" (https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf). The situation now is that mutations can be acquired at a high rate as well with the conventional techniques. This sets a new scene for comparing the new precision breeding techniques, in particular those based on CRISPR/Cas9, with the conventional mutation breeding techniques. Hence, with this development there has been a convergence between the new breeding techniques and the efficient use of TILLING principles in reverse genetics approaches. This applies to the general ability to achieve mutations in any gene of interest, but also to the speed of the process.

Despite the convergence between targeted genome editing and TILLING approaches there are still two main differences, which count in favor of NBT genome editing techniques: 1) precision – genome editing has only few constraints with respect to selection of the exact site of mutation in a gene, whereas TILLING is based on random mutations across the entire genome; 2) off-target mutations – genome editing can result in a few off-target mutations, whereas a high load of off-target mutations is an intrinsic property of conventional mutagenesis that has to be dealt with in plant breeding *via* extensive backcrossing strategies.

TABLE 1 | Mutagens commonly used in mutation breeding and in generation of TILLING mutant populations (Leitao, 2011; Mba et al., 2011; Sikora et al., 2011).

Category	Mutagen	Mutation type	Genotype
Physical treatment	X-rays	Dependent of dose: mixture of gene mutations and chromosomal mutations/ rearrangements	Point mutations.
	Gamma irradiation		Deletions/inversions of varying sizes. Translocations.
Chemical treatment	Alkylating mutagens: • MNU • EMS • ENU	Gene mutations	Alkylated base mispairing, typically leading to G/C→A/T transitions Few InDels
	NaN_3	Gene mutations	Both G/C→A/T og A/T→G/C transitions Few InDels

EMS, ethyl methanesulphonate; MNU, N-methyl-N-nitrosourea; ENU, 1-ethyl-1-nitrosourea; NaN_3, natriumazide, InDel, insertion/deletion.

Mutations Induced by the NBT Mutation Tools

As previously mentioned, the most widely used NBT mutation tool in plants is CRISPR/Cas9. This is mainly because it is highly efficient and easy to design and because it is possible by multiplexing to make more than one targeted mutation at a time (e.g. Bortesi and Fisher, 2015). However, ZNF, TALENs, and ODM are also currently used. ZFN was developed in 2003 (Bibikova et al., 2003), TALENs in 2011 (Bogdanove and Voytas, 2011) and CRISPR/Cas9 in 2012 (Jinek et al., 2012), so the SDN-tools are less than 20 years old. ODM, on the other hand, is a tool that has been used for a long time across mammalian, microbial, and plant systems to induce mutations at a specific site in the genome and ODM started to be successfully used in plants around 20 years ago (Breyer et al., 2009). Thus, NBT mutagenesis is almost 80 years younger than conventional mutagenesis.

Mechanism Behind the NBT Mutation Tools

The mechanism behind the precision of the ODM and SDN mutation tools are very different. ODM makes use of oligonucleotides (between 20 to 100 nucleotides in length) designed to be identical to a corresponding sequence in the plant genome except for one or a few altered nucleotides corresponding to the intended mutation (Breyer et al., 2009). The oligonucleotides bind to the complementary DNA sequence in the genome, thereby generating mismatches, which are repaired by the DNA repair system of the cell. As a result, a desired change is achieved at a specific site in the genome. The efficiency of this technique is, however, very low, and site-directed nucleases, especially the CRISPR/Cas tool, are therefore currently the preferred tool for creating NBT mutations.

SDNs are tools that can be designed to recognize and cleave at specific sites within a genome and thereby create a double strand break (DSB) at the targeted site. Mutations can then, prone to some error rate, be generated in the subsequent repair of the DSB performed by the cell's own DNA repair systems (Voytas, 2013). The DSB enables the creation of different types of mutations by harnessing the DSB repair pathways of the cell. The different types of mutations obtained by the two primary repair pathways, non-homologous end-joining and homologous recombination, are often referred to as SDN1 and SDN2, respectively.

The most commonly used repair pathway of DSBs is non-homologous end-joining (NHEJ) in which the broken DNA strands are just simply rejoined. When the rejoining is imprecise, deletions or insertions are introduced at the site of the DSB. If the SDN-tool is designed to make a DSB in a gene sequence, imprecise rejoining can inactivate the gene by changing the amino acid sequence reading frame.

The other main repair system of DSBs in cells is homologous recombination (HR). This repair requires the presence of a DNA fragment with sequence homology to either site of the DSB which can be used as a template for the HR repair. Specific nucleotide changes in the genomic sequence at the site of the DSB can then be achieved through HR by designing a DNA repair template with homologous sequences to either side of the DSB, but with the desired nucleotide changes at the site of the DSB. When the DNA repair template is delivered to the cell along with the SDN-tool, the template can be used for HR repair of the DSB and the template with the nucleotide changes will be incorporated into the chromosome, thereby specifically replacing one or a few nucleotides to other desired nucleotides. In this way, the genetic code of an amino acid can be changed to the code of another amino acid. Replacing a single amino acid in an enzyme often can alter the activity or specificity of the enzyme. Therefore, if already known which amino acid that has to be replace to achieve an improvement, SDN2 can be used to induce the corresponding specific nucleotide change.

Changing a single or a few nucleotides using SDN2 is, however, difficult as the delivery of the SDN-tool to the cell must be coordinated with the delivery of the DNA repair template. Thus, new approaches to overcome this hurdle are currently developed. Two base editing systems based on the CRISPR/Cas9 tool have recently been developed which can alter a particular nucleotide in a DNA sequence without the use of a DNA repair template (reviewed by (Shan and Voytas, 2018). One system can change cytosine (C·G) to thymine (T·A) (Zong et al., 2017) and the other adenine (A·T) to guanine (G·C) (Li et al., 2018). These systems have been shown to work effectively in important crop plants, such as tomato, canola, corn, rice, and wheat (Shan and Voytas, 2018).

Constrains of NBT Mutations With Respect to Target Site and Traceability

As compared to conventional mutagenesis, there are only few constraints when selecting the exact site for NBT mutations. Although only few there are some constrains, in particular for the CRISPR/Cas system. It consists of a Cas nuclease inducing the DSB and a chimeric RNA (gRNA) where the first 20 nucleotides (the guide sequence) can be made complementary to a 20-nucleotide genomic sequence located where the mutation is intended (Jinek et al., 2012). The gRNA strand and the Cas nuclease forms the RNP complex, and together they will find and bind to the complementary nucleotides in the genome. Here the Cas nuclease will cleave the DNA double strand but only if a protospacer adjacent motif (PAM sequence) is present just in front of the 20 bp targeted DNA sequence in the genomic sequence. The most commonly used Cas nuclease is spCas9 which originates from *Streptococcus pyogenes*. The PAM sequence for spCas9 is NGG. Although the NGG sequence is abundant in plant genomes, the requirement for a particular PAM sequence represents a restriction on where in the genome a DSB can be induced. However, to overcome this, new engineered spCas9 nucleases or CRISPR/Cas systems identified in other bacteria requiring other PAM sequences are now available and can be used in the absence of a wild type spCas9 PAM sequence at sites where a DSB is desired (Kleinstiver et al., 2015; Ran et al., 2015; Kleinstiver et al., 2016b; Kim et al., 2017; Amrani et al., 2018).

A key difference between conventional mutation breeding and NBT mutations is that the NBT mutation tools have to be delivered into the cells. For ODM, the oligonucleotides are transiently delivered to the cell and are degraded in the cells after induction of the specific mutation. The SDN-tools can be delivered to the plant cells as DNA constructs either using stable or transient transformation techniques. Although mutated primary

transformants generated by stable transformation contains the SDN DNA-construct there is most frequently no linkage between the site of insertion of the construct and the site of the mutation. Mutants without the DNA construct can therefore be selected in the subsequent generation after segregation. For CRISPR/Cas, it is also possible to deliver the CRISPR and the Cas as mRNA and guide RNA, respectively (Zhang et al., 2016) or to deliver a pre-assembled ribonucleoprotein (RNP-complex) (Woo et al., 2015). RNA and RNP delivery completely exclude any introduction and integration of foreign DNA into the plant.

The lack of foreign DNA in the NBT mutated plants complicates the traceability, which is required when NBT mutations are regulated as GMOs. Traditional GM plants normally holds a large piece of foreign DNA inserted randomly in the plant genome. Today, GM plants are detected by standard or real-time PCR that, depending on the primers used, can identify specific gene elements, gene constructs, and transformation events present in the plants. Knowledge about the sequences to be identified is a prerequisite for design of the primers. With respect to traceability of NBT mutations, it will not be possible to separate mutations resulting from SDN1, SDN2, or ODM from mutations induced spontaneously or by conventional mutagenesis even if information about the gene sequences is available. The same goes for base editing. This will complicate the control of crops imported from countries that do not regulate NBT mutated crops.

Off-Target Mutations Induced by NBT Tools

An often-mentioned concern about the ODM and SDN-tools is if mutations are generated at places in the genome where the tools were not intended to mutate. These so-called off-target mutations occur when the tool is capable of binding and inducing DSBs within sequences similar to the sequence which the tool was designed for (off-target sequences). Both ODM and all the SDN-tools may induce off-target mutations but the frequency is higher with the CRISPR/Cas9 tool (Zischewski et al., 2017). The reason for this is a less specific binding capacity. For CRISPR/Cas9, the recognition sequence is a 20-nucleotide sequence complementary to a 20-nucleotide genomic sequence located where the mutation is intended. Although a 20-nucleotide gRNA recognition sequence is long enough to occur only once in the vast majority of plant genomes, the specific binding is highest for the 8 to 12 nucleotides of the gRNA following the PAM sequence. This means that the gRNA can bind to sequences where there are mismatches between the gRNA and the plant DNA in the last 8 to 12 nucleotides (Hsu et al., 2013; Pattanayak et al., 2013; Cho et al., 2014).

It is difficult to make a general estimate of the off-target mutation frequency induced by the CRISPR/Cas9 tool in plants. In most of the CRISPR/Cas9 mutated crops developed, no analyzes have been performed for off-targets. Out of 1328 studies using CRISPR/Cas, TALENs, base editing, ZFN, and ODM, 252 of them investigated off-target mutations. In around 3% of the analyzed potential of-target sites, unintended mutations were detected (Modrzejewski et al., 2019).

Examples of studies where the CRISPR/Cas9 off-target mutation frequencies have been investigated by PCR amplification of the off-target sequences, restriction fragment analysis and/or sequencing and where off-target mutations have been identified are shown in **Table 2**. The studies included show off-target mutation frequencies at these sites ranging between 0% and 67.5%, depending on the targeted sequence and show that off-target mutations are often induced when there are mismatches at positions 8 to 20 from the PAM sequence.

Off-target mutation frequencies can also be estimated by whole-genome sequencing (WGS). In order to get maximum information from this method, the appropriate controls need to be included, revealing also the mutagenesis effect of tissue culture and CRISPR/Cas.

In a recent study in rice, such an approach was used to distinguish pre-existing mutations, spontaneous mutations, and mutations caused by tissue culture and *Agrobacterium*-mediated transformation from off-target mutations (Tang et al., 2018). No off-target mutations were found in plants edited by 11 out of 12 different Cas9-gRNA. The off-target sequences of the one Cas9-gRNA where off-target mutations were found also contained mismatches at positions 1 to 8 from the PAM sequence. This indicates that in order to avoid off-target mutations there should be at least two mismatches at positions 1 to 8 from the PAM sequence between the target sequence and any potential off-target sequences. However, the most surprising result of the study was that the highest frequency of mutations in the edited rice plants were created by the tissue culture process which caused 102 to 248 single nucleotide variations and 32 to 83 indels per mutated plant.

Similarly a study in cotton demonstrated that the most variations following Cas9-editing are due either to somaclonal variation or/and pre-existing/inherent variation from maternal plants, but not off-target effects (Li et al., 2019).

Despite the off-target mutations caused by NBT mutagenesis, non-planned mutations are still generated at much lower frequencies by the SDN-tools than by conventional mutation breeding. Here thousands of mutations may co-occur in every plant of a mutant TILLING population screened for a desired mutation (e.g. (Krasileva et al., 2017; Szarejko et al., 2017).

Precautions Against CRISPR/Cas Off-Target Mutations

Regardless of the very low SDN-based off-target mutation rates when compared to conventional mutagenesis, various strategies have been developed to further avoid or minimize off-target mutations by CRISPR/Cas. For plant species where the whole genome sequence is available, the main strategy is to design a very specific guide RNA sequence and to check for the presence of off-target sequences in the genome to which the guide RNA sequence could bind more non-specifically. Different software platforms have been developed to design guide RNA sequences which will very specifically bind to the sequence where the desired mutation is intended.

For plants where the genome has not yet been fully sequenced various strategies can be used to reduce the risk of off-target mutations. The CRISPR/Cas9 specificity can be improved by increasing the number of nucleotides required to recognize corresponding nucleotides in the plant genome. This can be done using the Cas9 nickase or Cas9 FokI fusion proteins strategies,

TABLE 2 | Examples of studies where off-target mutations induced by CRISPR/Cas9 were identified by PCR/RE and/or sequencing.

Reference	Species	Delivery method	Potential off-target sites	Homologous genes
(Xie and Yang, 2013)	Rice	Stabile CRISPR/Cas9	Off-target mutation in one of three potential off-target sites containing a mismatch at position 11 and 15 from the PAM with a mutation frequency of 1.6%	
(Endo et al., 2015)	Rice	Stabile CRISPR/Cas9		For one gRNA, off-target mutations were investigated in 3 homologous genes. One gene contained mismatches at positions 7, 16, and 18 from the PAM and showed no off-target mutations in 31 plants. Another gene contained a mismatch at position 18 from the PAM and showed off-target mutations in 19 out of 31 (61.3%) plants. The third gene contained mismatches at positions 10 and 16 from the PAM and showed off-target mutations in 17 (54.8%) out of 31 plants
(Zhang et al., 2016)	Wheat	Stable CRISPR/Cas9 or Transient DNA CRISPR/Cas9 or Transient RNA CRISPR/Cas9	For one gRNA the software predicted eight potential off-target sites containing different mismatches at positions within the 20 to 6 bp from the PAM. No off-target mutations were identified in a total of 67 regenerated mutants generated by either delivery method. For another gRNA the software predicted 24 potential off-target sites containing different mismatches at positions within 20 to 1 bp from the PAM. No off-target mutations were identified in a total of 101 regenerated mutants generated by transient DNA delivery.	For one gRNA, off-target mutations were investigated in one homeologues gene with a mismatch at position 9 from the PAM. For stabile delivery with DNA, transient delivery with DNA. and transient delivery with RNA, off target mutations were identified in 2.0%, 2.3% and 0.4% of the regenerated mutants, respectively.
(Li et al., 2016)	Rice	Stable CRISPR/Cas9	For four different gRNAs, two potential off-target sites were investigated. Within these eight sites, off-target mutations were identified at three sites containing mismatches at position 13, 14 + 16–20, and 8 from the PAM with mutation frequencies of 67.5%, 2.5% and 47.5%, respectively.	

which both greatly reduce the number of possible off-target sequences [reviewed by (Bortesi and Fischer, 2015)]. Another strategy is to use the newly developed spCas9-HF or the Cas12a nuclease, both possessing higher specificity (Kleinstiver et al., 2016a; Strohkendl et al., 2018). The delivery method used for the CRISPR/Cas9 tool to the cells also greatly influences the frequency of off-target mutations. Studies have shown that delivery of the CRISPR/Cas9 tool as RNP complexes reduce the number of off-target mutations since RNP complexes degrade much faster in the cell than DNA constructs (Kim et al., 2014; Liang et al., 2017).

RNP delivery seems to be one of the most promising tools for reducing off-targets. The RNP delivery is, however, currently only possible by protoplast transfection or by particle bombardment (Woo et al., 2015; Liang et al., 2017). Currently, this puts some limitations on a broad use of RNP as regeneration of plants from protoplasts is only possible from rather few plant species and highly efficient protocols for particle bombardment and plant regeneration is limited to a few species. Future developments might increase the number of plant species where RNP delivery is possible and make RNPs the preferred way of CRISPR/Cas delivery. Moreover, the number of plant species with fully sequenced genomes is constantly increasing and expands the number of plant species where maximum specific guide RNA sequences can be designed.

DISCUSSION AND CONCLUSIONS

The status of new breeding technologies (in particular SDN1 tools) with respect to the EU GMO legislation is important for the possibilities to exploit the potentials of the technologies in future European plant breeding. The ruling of the EU Court of

Justice in July 2018 stating that organisms obtained by the new mutation techniques are not exempt from the legislation on the deliberate release of GMOs, makes it difficult, if not impossible, for plant breeders to make use of the new techniques, due to heavy costs associated with the approval of GM varieties (Eriksson et al., 2018). Realistically, only big companies can afford the costs and, hence, only these companies can probably make commercial use of the new genome editing technologies. On short terms, the influence on the European plant breeding industry, in particular small and medium size enterprises (SMEs), might not be strong although quite a number of SMEs may have stopped their own SDN projects after this ruling. However, in the longer perspective, this industry will probably stand weak in the competition with countries outside EU, like the US where USDA APHIS has formulated a policy in which crops that contain single nucleotide changes or deletions of any size would no longer be a regulated article, and Argentina and Brazil which have installed a process that results in that certain SDN plants are not subject to the provisions of their GMO legislation.

Paradoxically, mutant plants can now be achieved with mutagenesis methods exempted from the GM legislation just as fast as with the SDN1 techniques. Hence, with respect to targeting and speed a convergence between conventional mutagenesis and the SDN1 techniques has occurred. The two major differences are the precision and the number of off-target mutations, both of which favour the SDN1 methods.

With the current status of the EU legislation of plants with NBT mutations, reluctance by private industry to embark on projects implementing these techniques in generation of new varieties will probably persist. Already now, Europe falls behind with respect to patenting within the area of CRISPR-based plant biotechnology (Martin-Laffon et al., 2019). However, the techniques could still be used with success in research projects that address the molecular genetics of crop traits. Hand-in-hand with the use of classical mutation techniques through screening of TILLING populations NBT mutations could be utilized indirectly, although not optimally, in the modulation of crop traits. First, the precision and specificity of the NBT mutations could be used to clearly define strong mutation targets, without the genetic noise that would be present in classical mutation strategies. Subsequently, the defined efficient mutations could be re-constructed/re-gained by the use of classical mutation techniques. This is a cumbersome process, but still applicable, in particular due to the development of efficient methods to build mutant (TILLING) populations and efficient methods to screen them for mutations of specific target genes (Jankowicz-Cieslak et al., 2017).

The development of crop varieties usually takes many years and, thus, the effects on the market and in agriculture will have an equivalent lag. For proper exploitation, it is therefore important that implementation of the new precision breeding techniques is started now, maybe in strategies in combination with TILLING approaches as outlined above. The fear, however, could be that the decision by the EU court will still make the industry reluctant to go into research and development directed toward the use of the new techniques. This would only aggravate the long term weakening of the European breeding industry in the global competition.

For some crops and traits, in particular ornamentals and garden/vegetable seeds, new cultivars have a short developmental horizon, e.g., when it comes to developing new flower colours. Since the market of these is global, the impact of the new techniques on Europe can come on rather short terms, if restrictions on their use, as expected, will be limited in Asia, South America, Canada, and the US. This raises the issues of detection of genetic modifications introduced by the new techniques. In Europe, they are regulated according to the current EU GMO legislation and, hence, subject to strict approval, but it is close to impossible to make unambiguous tests for the introduced mutations, since there are no marks distinguishing them from natural mutations/variants. This situation will get even worse on longer terms, when varieties of major European crops with new NBT mutation induced traits can enter the European market from the surrounding world and be crossed with locally developed varieties. From the regulatory aspect, this situation will not be sustainable and thus unacceptable for the European plant breeding industry. Long-term stability in this area calls for clarifications at the political level of EU legislation.

AUTHOR CONTRIBUTIONS

IH, PG and HB contributed equally to the manuscript.

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REFERENCES

Amrani, N., Gao, X. D., Liu, P., Edraki, A., Mir, A., Ibraheim, R., et al. (2018). NmeCas9 is an intrinsically high-fidelity genome-editing platform. *Genome Biol.* 19, 214. doi: 10.1186/s13059-018-1591-1

Bibikova, M., Beumer, K., Trautman, J. K., and Carroll, D. (2003). Enhancing gene targeting with designed zinc finger nucleases. *Science* 300, 764. doi: 10.1126/science.1079512

Bogdanove, A. J., and Voytas, D. F. (2011). TAL effectors: customizable proteins for DNA targeting. *Science* 333, 1843–1846. doi: 10.1126/science.1204094

Bolon, Y. T., Haun, W. J., Xu, W. W., Grant, D., Stacey, M. G., Nelson, R. T., et al. (2011). Phenotypic and genomic analyses of a fast neutron mutant population resource in soybean. *Plant Physiol.* 156, 240–253. doi: 10.1104/pp.110.170811

Bortesi, L., and Fischer, R. (2015). The CRISPR/Cas9 system for plant genome editing and beyond. *Biotechnol. Adv.* 33, 41–52. doi: 10.1016/j.biotechadv.2014.12.006

Breyer, D., Herman, P., Brandenburger, A., Gheysen, G., Remaut, E., Soumillion, P., et al. (2009). Commentary: Genetic modification through oligonucleotide-mediated mutagenesis. A GMO regulatory challenge? *Environ. Biosafety Res.* 8, 57–64. doi: 10.1051/ebr/2009007

Burkart-Waco, D., Tsai, H., Ngo, K., Henry, I. M., Comai, L., and Tai, T. H., (2017). "*Biotechnologies for Plant Mutation Breeding: Protocols*," in *Next-Generation Sequencing for Targeted Discovery of Rare Mutations in Rice*. Eds.

Jankowicz-Cieslak, J., Tai, T. H., Kumlehn, J., and Till., B. J. (Cham: Springer International Publishing), 323–340. doi: 10.1007/978-3-319-45021-6_20

Cho, S. W., Kim, S., Kim, Y., Kweon, J., Kim, H. S., Bae, S., et al. (2014). Analysis of off-target effects of CRISPR/Cas-derived RNA-guided endonucleases and nickases. *Genome Res.* 24, 132–141. doi: 10.1101/gr.162339.113

Court-of-Justice-of-the-European-Union. (2018). Organisms obtained by mutagenesis are GMOs and are, in principle, subject to the obligations laid down by the GMO Directive. *PRESS RELEASE*.

Endo, M., Mikami, M., and Toki, S. (2015). Multigene knockout utilizing Off-target mutations of the CRISPR/Cas9 system in rice. *Plant Cell Physiol.* 56, 41–47. doi: 10.1093/pcp/pcu154

Eriksson, D., Brinch-Pedersen, H., Chawade, A., Holme, I. B., Hvoslef-Eide, T. A. K., Ritala, A., et al. (2018). Scandinavian perspectives on plant gene technology: applications, policies and progress. *Physiol. Plant* 162, 219–238. doi: 10.1111/ppl.12661

Hasan, M. M., Rafii, M. Y., Ismail, M. R., Mahmood, M., Rahim, H. A., Alam, M. A., et al. (2015). Marker-assisted backcrossing: a useful method for rice improvement. *Biotechnol. Biotechnol. Equip.* 29, 237–254. doi: 10.1080/13102818.2014.995920

Haun, W., Coffman, A., Clasen, B. M., Demorest, Z. L., Lowy, A., Ray, E., et al. (2014). Improved soybean oil quality by targeted mutagenesis of the fatty acid desaturase 2 gene family. *Plant Biotechnol. J.* 12, 934–940. doi: 10.1111/pbi.12201

Hsu, P. D., Scott, D. A., Weinstein, J. A., Ran, F. A., Konermann, S., Agarwala, V., et al. (2013). DNA targeting specificity of RNA-guided Cas9 nucleases. *Nat. Biotechnol.* 31, 827–832. doi: 10.1038/nbt.2647

Jankowicz-Cieslak, J., Mba, C., and Till, B. J., (2017). "*Biotechnologies for Plant Mutation Breeding: Protocols*," in *Mutagenesis for Crop Breeding and Functional Genomics*. Eds. Jankowicz-Cieslak, J., Tai, T. H., Kumlehn, J., and Till, B. J. (Cham: Springer International Publishing), 3–18. doi: 10.1007/978-3-319-45021-6_1

Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J. A., and Charpentier, E. (2012). A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science* 337, 816–821. doi: 10.1126/science.1225829

Kim, E., Koo, T., Park, S. W., Kim, D., Kim, K., Cho, H.-Y., et al. (2017). *In vivo* genome editing with a small Cas9 orthologue derived from Campylobacter jejuni. *Nat. Commun.* 8, 14500. doi: 10.1038/ncomms14500

Kim, S., Kim, D., Cho, S. W., Kim, J., and Kim, J. S. (2014). Highly efficient RNA-guided genome editing in human cells via delivery of purified Cas9 ribonucleoproteins. *Genome Res.* 24, 1012–1019. doi: 10.1101/gr.171322.113

Kleinstiver, B. P., Pattanayak, V., Prew, M. S., Tsai, S. Q., Nguyen, N. T., Zheng, Z., et al. (2016a). High-fidelity CRISPR–Cas9 nucleases with no detectable genome-wide off-target effects. *Nature* 529, 490–495. doi: 10.1038/nature16526

Kleinstiver, B. P., Prew, M. S., Tsai, S. Q., Topkar, V. V., Nguyen, N. T., Zheng, Z., et al. (2015). Engineered CRISPR-Cas9 nucleases with altered PAM specificities. *Nature* 523, 481–485. doi: 10.1038/nature14592

Kleinstiver, B. P., Tsai, S. Q., Prew, M. S., Nguyen, N. T., Welch, M. M., Lopez, J. M., et al. (2016b). Genome-wide specificities of CRISPR-Cas Cpf1 nucleases in human cells. *Nat. Biotechnol.* 34, 869–874. doi: 10.1038/nbt.3620

Krasileva, K. V., Vasquez-Gross, H. A., Howell, T., Bailey, P., Paraiso, F., Clissold, L., et al. (2017). Uncovering hidden variation in polyploid wheat. *Proc. Natl. Acad. Sci.* 114, E913–E921. doi: 10.1073/pnas.1619268114

Leitao, J. M. (2011). "*Plant mutation breeding and biotechnology*," in *Chemical mutagenesis*. Eds. Shu, Q. Y., Forster, B. P., and Nakagawa, H. (Wallingford: CABI), 135–158. doi: 10.1079/9781780640853.0135

Li, C., Zong, Y., Wang, Y., Jin, S., Zhang, D., Song, Q., et al. (2018). Expanded base editing in rice and wheat using a Cas9-adenosine deaminase fusion. *Genome Biol.* 19, 59. doi: 10.1186/s13059-018-1443-z

Li, J., Manghwar, H., Sun, L., Wang, P., Wang, G., Sheng, H., et al. (2019). Whole genome sequencing reveals rare off-target mutations and considerable inherent genetic or/and somaclonal variations in CRISPR/Cas9-edited cotton plants. *Plant Biotechnol. J.* 17, 858–868. doi: 10.1111/pbi.13020

Li, M., Li, X., Zhou, Z., Wu, P., Fang, M., Pan, X., et al. (2016). Reassessment of the four yield-related genes Gn1a, DEP1, GS3, and IPA1 in Rice Using a CRISPR/Cas9 System. *Front. Plant Sci.* 7, 377. doi: 10.3389/fpls.2016.00377

Liang, Z., Chen, K., Li, T., Zhang, Y., Wang, Y., Zhao, Q., et al. (2017). Efficient DNA-free genome editing of bread wheat using CRISPR/Cas9 ribonucleoprotein complexes. *Nat. Commun.* 8, 14261. doi: 10.1038/ncomms14261

Lundqvist, U. (2014). Scandinavian mutation research in barley – a historical review. *Hereditas* 151, 123–131. doi: 10.1111/hrd2.00077

Lusser, M., Parisi, C., Plan, D., and Rodríguez-Cerezo, E. (2012). Deployment of new biotechnologies in plant breeding. *Nat. Biotecnol.* 30, 231–239. doi: 10.1038/nbt.2142

Martin-Laffon, J., Kuntz, M., and Ricroch, A. E. (2019). Worldwide CRISPR patent landscape shows strong geographical biases. *Nat. Biotechnol.* 37, 613–620. doi: 10.1038/s41587-019-0138-7

Mba, C. (2013). Induced mutations unleash the potentials of plant genetic resources for food and agriculture. *Agronomy* 3, 200. doi: 10.3390/agronomy3010200

Mba, C., Afza, R., and Shu, Q. Y., (2011). "*Plant mutation breeding and biotechnology*," in *Mutagenic radiations: X-rays, ionizing particles and ultraviolet*. Eds. Shu, Q. Y., Forster, B. P., and Nakagawa, H. (Wallingford: CABI), 83–90. doi: 10.1079/9781780640853.0083

Mccallum, C. M., Comai, L., Greene, E. A., and Henikoff, S. (2000). Targeting induced local lesions in genomes (TILLING) for plant functional genomics. *Plant Physiol.* 123, 439–442. doi: 10.1104/pp.123.2.439

Modrzejewski, D., Hartung, F., Sprink, T., Krause, D., Kohl, C., and Wilhelm, R. (2019). What is the available evidence for the range of applications of genome-editing as a new tool for plant trait modification and the potential occurrence of associated off-target effects: a systematic map. *Environ. Evid.* 8, 27. doi: 10.1186/s13750-019-0171-5

Pattanayak, V., Lin, S., Guilinger, J. P., Ma, E., Doudna, J. A., and Liu, D. R. (2013). High-throughput profiling of off-target DNA cleavage reveals RNA-programmed Cas9 nuclease specificity. *Nat. Biotechnol.* 31, 839–843. doi: 10.1038/nbt.2673

Ran, F. A., Cong, L., Yan, W. X., Scott, D. A., Gootenberg, J. S., Kriz, A. J., et al. (2015). *In vivo* genome editing using Staphylococcus aureus Cas9. *Nature* 520, 186–191. doi: 10.1038/nature14299

Schaart, J. G., Van De Wiel, C. C. M., Lotz, L.a.P., and Smulders, M. J. M. (2016). Opportunities for products of new plant breeding techniques. *Trends Plant Sci.* 21, 438–449. doi: 10.1016/j.tplants.2015.11.006

Shan, Q., and Voytas, D. F. (2018). Editing plant genes one base at a time. *Nat. Plants* 4, 412–413. doi: 10.1038/s41477-018-0177-y

Shan, Q., Zhang, Y., Chen, K., Zhang, K., and Gao, C. (2015). Creation of fragrant rice by targeted knockout of theOsBADH2gene using TALEN technology. *Plant Biotechnol. J.* 13, 791–800. doi: 10.1111/pbi.12312

Sikora, P., Chawade, A., Larsson, M., Olsson, J., and Olsson, O. (2011). Mutagenesis as a tool in plant genetics, functional genomics, and breeding. *Int. J. Plant Genomics* 2011, 13. doi: 10.1155/2011/314829

Stadler, L. J. (1928). Genetic Effects of X-Rays in Maize. *Proc. Natl. Acad. Sci.* 14, 69–75. doi: 10.1073/pnas.14.1.69

Strohkendl, I., Saifuddin, F. A., Rybarski, J. R., Finkelstein, I. J., Russell, R. (2018). Kinetic basis for DNA target specificity of CRISPR-Cas12a. *Mol. Cell* 71, 816–824. doi: 10.1016/j.molcel.2018.06.043

Szarejko, I., Szurman-Zubrzycka, M., Nawrot, M., Marzec, M., Gruszka, D., Kurowska, M., et al. (2017). "*Biotechnologies for Plant Mutation Breeding: Protocols*," in *Creation of a TILLING Population in Barley After Chemical Mutagenesis with Sodium Azide and MNU*. Eds. Jankowicz-Cieslak, J., Tai, T. H., Kumlehn, J., and Till., B. J. (Cham: Springer International Publishing), 91–111. doi: 10.1007/978-3-319-45021-6_6

Szurman-Zubrzycka, M., Chmielewska, B., Gajewska, P., and Szarejko, I., (2017). "*Biotechnologies for Plant Mutation Breeding: Protocols*," in *Mutation Detection by Analysis of DNA Heteroduplexes in TILLING Populations of Diploid Species*. Eds. Jankowicz-Cieslak, J., Tai, T. H., Kumlehn, J., and Till., B. J. (Cham: Springer International Publishing), 281–303. doi: 10.1007/978-3-319-45021-6_18

Szurman-Zubrzycka, M. E., Zbieszczyk, J., Marzec, M., Jelonek, J., Chmielewska, B., Kurowska, M. M., et al. (2018). HorTILLUS—A Rich and Renewable Source of induced mutations for forward/reverse genetics and pre-breeding programs in barley (Hordeum vulgare L.). *Front. Plant Sci.* 9, 216. doi: 10.3389/fpls.2018.00216

Tang, X., Liu, G., Zhou, J., Ren, Q., You, Q., Tian, L., et al. (2018). A large-scale whole-genome sequencing analysis reveals highly specific genome editing by both Cas9 and Cpf1 (Cas12a) nucleases in rice. *Genome Biol.* 19, 84. doi: 10.1186/s13059-018-1458-5

Voytas, D. F. (2013). Plant genome engineering with sequence-specific nucleases. *Annu. Rev. Plant Biol.* 64, 327–350. doi: 10.1146/annurev-arplant-042811-105552

Woo, J. W., Kim, J., Kwon, S. I., Corvalán, C., Cho, S. W., Kim, H., et al. (2015). DNA-free genome editing in plants with preassembled CRISPR-Cas9 ribonucleoproteins. *Nat. Biotechnol.* 33, 1162–1164. doi: 10.1038/nbt.3389

Xie, K., and Yang, Y. (2013). RNA-guided genome editing in plants using a CRISPR–cas system. *Mol. Plant* 6, 1975–1983. doi: 10.1093/mp/sst119

Zhang, Y., Liang, Z., Zong, Y., Wang, Y., Liu, J., Chen, K., et al. (2016). Efficient and transgene-free genome editing in wheat through transient expression of CRISPR/Cas9 DNA or RNA. *Nat. Commun.* 7, 12617. doi: 10.1038/ncomms12617

Zischewski, J., Fischer, R., and Bortesi, L. (2017). Detection of on-target and off-target mutations generated by CRISPR/Cas9 and other sequence-specific nucleases. *Biotechnol. Adv.* 35, 95–104. doi: 10.1016/j.biotechadv.2016.12.003

Zong, Y., Wang, Y., Li, C., Zhang, R., Chen, K., Ran, Y., et al. (2017). Precise base editing in rice, wheat and maize with a Cas9-cytidine deaminase fusion. *Nat. Biotechnol.* 35, 438–440. doi: 10.1038/nbt.3811

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The Economics of Regulating New Plant Breeding Technologies - Implications for the Bioeconomy Illustrated by a Survey Among Dutch Plant Breeders

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New plant breeding technologies (NPBTs) are increasingly used for developing new plants with novel traits. The science tells us that those plants in general are as safe as than those once developed using "conventional" plant breeding methods. The knowledge about the induced changes and properties of the new plants by using NPBTs is more precise. This should lead to the conclusion that plants developed using NPBTs should not be regulated differently than those developed using "conventional" plant breeding methods. This contribution discusses the economics of regulating new plant breeding technologies. We first develop the theoretical model and elaborate on the different regulatory approaches being used and compare their advantages and disadvantages. Then we provide a perspectives on EU regulation around mutagenesis-based New Plant Breeding Techniques (NPBT), formed by new insights from a survey among Dutch plant breeding companies. The survey measures the attitude of breeding companies towards the ruling of the EU Court of Justice that subjected the use of CRISPR-Cas in the development of new plant varieties under the general EU regulations around GMOs. The results show that plant breeders experience a financial barrier because of the ruling, with perceived negative impact on competitiveness and investments in CRISPR-Cas as a result. The degree of negative impact differs however significantly among seed-sectors and company sizes. One of the most striking results was the relative optimism of companies in the sector about more lenient legislation in the next five years, despite the stated negative effects.

Keywords: CRISPR-Cas, regulation, plant breeding sector, impact, Dutch plant breeders, Court of Justice of the European Union, genetically modified organism, new plant breeding technologies

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INTRODUCTION

The design of a regulatory regime for new plant breeding technologies (NPBTs) is under discussion in the European Union (EU), the United States (US), Canada, and many other parts of the world. In particular, it is being discussed whether or not they should be regulated similarly to genetically modified organisms (GMOS) or non-GMOs, or whether they need special regulations (Eriksson et al., 2019). In the case of the EU, since NPBTs include a wide range of methods, some applications

will result in crops to be considered a GMO under the EU regulatory system, and others not (see Sprink et al., 2016 for an overview). Even if they are considered to be a GMO, simplified approval processes might be possible (Purnhagen et al., 2018).

The EU policies on NPBTs will have implications for international trade and regulatory systems in other countries (Wesseler et al., 2017), and vice versa. Further, regulatory approaches affect the duration and cost of the approval process with related implications for investments in plant breeding (Kalaitzandonakes et al., 2007; Smart et al., 2017; Smyth et al., 2017).

Stringent regulations of GMOs have impacts expanding beyond agriculture. It is often presumed that the stringent regulations of GMOs in the EU only affect the agriculture and food sector, but not the medical sector and other parts of the bioeconomy. While this line of reasoning may apply to consumer attitudes toward biotechnology, it is misleading in a broader context. There is some evidence of negative spill-overs of the presumed stringent regulations on clusters of regularly interspaced short palindromic repeat (CRISPR)-based technologies in the EU to the medical as well as other sectors. A recently published survey (Martin-Laffon, 2019) on the CRISPR-patent landscape shows patent applications in the EU are substantially lacking behind other regions in the world, and not only in agriculture but also in the fields of medical, industrial, and technical applications (**Table 1**).

In this contribution the economics of regulating NPBTs and their implications are presented and discussed. First, a general economic model of regulation and its implications for investment in NPBTs is introduced, followed by a presentation of the potential implications based on a recent survey of the Dutch plant breeding sector.

The Economics of Regulating New Plant Breeding Technologies

The demand for regulating NPBTs originates from concerns about potential negative implications for human health and the environment. There are two strategies for regulation that can be combined. One is imposing *ex-ante* regulatory standards for prior approval before commercialization. Second is *ex-post* liability rules to compensate for damages and to penalize non-compliance with *ex-ante* regulations. Economic research analyzes the mixture of these two regulatory approaches (see e.g., Kolstad et al., 1990).

TABLE 1 | Number of CRISPR Patent Families by Technical Fields and EU Share.

Technical field	Total number	European Union	
		No.	%
Agricultural	374	18	4.8
Industrial	192	23	12.0
Medical	614	19	3.1
Technical improvement	1,052	76	7.7

Source: based on data published in Martin-Laffon et al. (2019). Regional identification of patent applications has been done by first priority date.

The advantage of *ex-ante* regulatory standards is that potential damage can be reduced before damage actually happens. The disadvantage is that those standards apply uniformly without recognizing heterogeneity among applications as well as applicants. Some applications and/or applicants might be over-regulated while others might be under-regulated (e.g., Shavell, 1984). The main problem for *ex-ante* regulatory standards is caused by information asymmetries between the regulator and the firm. The firm has more detailed knowledge about the product than the regulator. Firms in general are required to provide a set of standard regulatory information, but regulators have the option to seek additional case-specific information. This option can increase the cost and delay approval. The approval process may entail performance standards that have to be followed, which can in some cases be prohibitively high, such as in the case of some GMO coexistence regulations (Beckmann et al., 2010).

Ex-post liability applies when companies face legal challenges from externalities of e.g., NPBTs, such as health or environmental claims. Those threats provide incentives for companies to take *ex-ante* voluntary precautions to address potential health and environmental safety issues. Shleifer (2010) notes that perfect *ex-post* liability regulations would be sufficient to ensure that users of NPBTs do not expose themselves to liability greater than the damage costs they would face. If the penalties correspond to social costs, then its outcomes are optimal, which is consistent with Coase (1960). However, a perfect system requires that the damage and the liable party can be correctly identified and that juries are not corrupt or biased. When this is not the case, because of imperfect information and financial considerations, a policy combining *ex-ante* regulatory standards and *ex-post* liability systems can improve social welfare (Kolstad et al., 1990). The challenge is to identify the right combination of *ex-ante* regulatory standards and *ex-post* liability rules.

The incentive for firms to invest in NPBTs largely depends on the net benefits of the investment, which are influenced by *ex-ante* regulatory standards and *ex-post* liability. In making an investment decision, the product life can be divided in four important phases: research and development (R&D); approval (A); marketing (M); post-marketing liability (L). All these phases are characterized by uncertainty over the benefits and costs as well as by their time length (see e.g., Purnhagen and Wesseler, 2019).

The R&D phase includes multiple uncertainties including the probability of success and the time taken to obtain it, the costs of testing new ideas, as well as upscaling them. These costs are affected by regulation, as compliance with regulations may extend the duration of research in the lab and the field, and increase the costs. Some countries even have strict field trial requirements that are often technically infeasible and economically unviable (Kuntz, 2012). The requirement to publicize the location of field trials in some EU member states, e.g., has resulted in public protests making it almost impossible for companies to conduct those trials.

The approval process can also add substantial costs. Research shows that the direct costs of the approval process varies substantially, from a few thousand USD to several millions (Smyth et al., 2017), depending on the regulatory environment,

while the time length of the approval process also varies widely (Jin et al., 2019). The time length of the approval process adds additional costs for plant breeders as it delays market access, but also for other participants in the food and feed supply chain, caused by the asynchronicity in approval at country level affecting international trade (European Commission, 2007; Backus et al., 2009).

The production and marketing of approved products also faces regulations. The coexistence regulations in the EU may severely limit where GMO traits can be produced and thus increase production costs. Food and feed products derived from the use of NPBTs also need to comply, as other food and feed products, with the EU laws on food and feed (Purnhagen, 2019). Furthermore, many countries have implemented labeling policies for GMOs that make GMOs differentiated products from non-GMOs (Castellari et al., 2018). This poses an additional challenge when there is no detectable difference between NPBTs and "conventional" products for international trade, product differentiation *via* labeling, and coexistence.

In summary, the regulatory environment effects the costs and benefits of investments in NPBTs. As the regulatory environment differs by country and region, this provides different incentives for plant breeders for their choice of investments.

Economic Implications of Regulation and Delayed Approvals for Plant Breeding: The Case of the European Union

In the summer of 2018, the Court of Justice of the EU ruled that on CRISPR-based plant breeding technologies are not immediately exempted from existing EU regulation of GMOs (Purnhagen et al., 2018). The ruling frustrated many in the field of biotechnology and led experts to speculate about its potential effects on EU-based plant breeders. These concerns relate to the cost of approval procedures and their potential negative impact on competitiveness and firms' investments in CRISPR-based technologies (Callaway, 2018). They include wider implications for food security (Zaidi et al., 2019) and the development of the bioeconomy, particularly in Europe (Wesseler and von Braun, 2017).

In the EU, cultivation of genetically modified plants is nearly negligible due to procedures required for bringing plants classified as GMOs to market. In 2017, only 131,535 (James, 2017) of the 11.9 million total hectares for permanent crops (Eurostat, 2018) were planted with the one genetically modified crop approved for cultivation, an insect-resistant maize. It was expected that the introduction of new more precise and nature-like plant breeding techniques, especially CRISPR-Cas, would overcome the resistance to the application of modern biotechnology in plant breeding and unleash the potential of improved plant varieties (Eriksson, 2019). The recent ruling by the EU's highest court that requires plants developed by these mutagenesis-based modification methods to follow the approval process for GMOs, therefore came as a blow (Purnhagen et al., 2019). First of all, the theoretical model suggests the EU GMO approval procedure to be a major barrier for the use of CRISPR-Cas in plant breeding. Besides that, it is expected that the nature of the approval procedure has negative consequences for the investments in CRISPR-Cas technique. Furthermore, one can expect the decision to lead to competitive disadvantage for plant breeding companies. A recent survey of Dutch plant breeding companies gives a first empirical insight on the impact of the ruling.

Among the EU-members, the Netherlands has an especially strong position in the development, propagation and trade of reproduction materials. Around 40% of all globally traded vegetable seeds and 60% of traded seed potatoes are of Dutch origin. The Dutch seed sector also contributes 60% of applications for plant breeder rights (Government of the Netherlands, 2017), making it a core location for the development of plant reproduction materials in the EU. These characteristics make the sector a sensible object of study for a first assessment of the expected effects and implications of the ruling.

MATERIALS AND METHODS

The population we consider consists of companies that are affiliated with PLANTUM, the association that serves the interests of around 350 companies in the plant breeding sector in the Netherlands. In 2011, of the then 400 Dutch companies active in the plant breeding sector, 385 were affiliated with PLANTUM (Kokcis et al., 2013). The high coverage of the PLANTUM database shows that this population includes 87.5 per cent of Dutch plant breeding companies.

To judge the representativeness of the sample, usually a description of the population should be sketched. Unfortunately, no quantitative overview exists of the Dutch plant breeding sector, categorized by seed sector. However, considering the former high coverage ratio of the PLANTUM company database, the population we consider can be assumed to cover a vast majority of the population. Within the online company database the companies which are categorized under "agriculture" (31 units), "fruit trees" (1 unit), "*in vitro laboratoria*" (9 units), "vegetable seeds" (25 units), and a selection of the relevant actors (9 out of 22) within "other services" have been considered to be part of the population we consider. This led to a population of 75 units. Due to the absence of contact details, three units had to be removed (all in "agriculture") resulting in a sampling population of 72 (**Table 2**).

The online survey was distributed by e-mail to the general contact address of the company. The guiding text asked to forward the survey to the relevant R&D manager within the company. Whenever the address was available, the survey was directly sent to the relevant R&D manager or department. The survey was open for response from 7th to 20th February 2019. During the course of the survey, two reminders were sent to the units in the sample.

The survey starts with four questions on the profile of the company in terms of size, seed sector, country of headquarter and main market. The number of employees was chosen as the measure of company size, since it is expected to lead to more reliable data than sales. The European Commission (EC) definition of company size, defined in EU Recommendation 2003/361, was followed.

TABLE 2 | Distribution of the population (sample) across the defined categories of seed sectors and company sizes.

	Seed potato	Vegetables	Agriculture	Fruit trees	*In vitro* Labs	Other	Multi	Total	Share (%)
Micro (<10 empl.)	2 (3)	3 (1)	1 (0)			2 (0)	1 (1)	9 (5)	13 (15)
Small (10 to 49 empl.)	3 (1)	10 (4)	4 (2)	1 (0)	5 (0)	3 (2)	1 (0)	27 (9)	38 (27)
Medium (50 to 249 empl.)	1 (1)	4 (2)	2 (2)		2 (2)	3 (0)	0 (2)	12 (9)	17 (27)
Large (250+ empl.)	4 (2)	8 (5)	8 (3)		2 (0)	1 (0)	1 (0)	24 (10)	33 (30)
Total	10 (7)	25 (12)	15 (7)	1 (0)	9 (2)	9 (2)	3 (3)	72 (33)	
Share (%)	14 (21)	35 (36)	21 (21)	1 (0)	13 (6)	13 (6)	4 (9)		100 (100)

Categorization is based on company profile as publicly provided by the companies. Company-size categories as defined in EU recommendation 2003/361. Differences in company sizes are the result of the categorization by companies themselves, as reported in brackets, as opposed to the categorization based on publicly available information.

The respondents were also requested to state their understanding of the impact of regulation on the company. This way, any severe bias due to a respondent's lack of knowledge could be identified and possibly corrected, *ex post*. The body of the survey consisted of eight questions about: 1) the respondents overview on the impact of regulatory policies on the company; 2) the role of CRISPR-Cas within the company; 3) the effects of the structure of the current GMO regulatory framework on investment in CRISPR-Cas; the impact of the recent court ruling on 4) the investments and 5) the competitiveness of the company; 6) the use of alternative technologies; 7) the prospects of changes in EU legislation and 8) its effects on the Dutch plant breeding sector. These questions were answered on a five-point Likert-scaled range of response possibilities, ranging from *strongly disagree* to *strongly agree*. For some questions a *not relevant*-option was provided. Lastly, there was room for additional comments. The Likert-scale is one of the most used and reliable scales to measure opinions and underlying motives of behavior (Burns and Bush, 2008). Nevertheless, the correct way to deal with the data resulting from surveys with a Likert-type scale has often been debated. Specifically, the disagreement addresses whether resulting data should be dealt with as ordinal or cardinal measurements. This has implications for the statistical methods that need to be used in the analysis of the data. Although it is rather customary to deal with such data as being cardinal, the intervals cannot be assumed to be equal from a theoretical perspective (Sullivan and Artino, 2013). Considering this, and further assumptions on the structure of the data (e.g., sample size and normality), in this research it seems better justified to regard the data as being ordinal for statistical analysis. Therefore, non-parametric tests will be applied. However, it should be noted that averages will be used in the graphical presentation of the data (**Figure 1**). Averages are preferred in the graphical presentation, because they pose less risk for extreme (i.e., misleading) results compared to other central tendencies (e.g., modus). One should, however, consider the ordinal character of the data when directly comparing means of subgroups. An overview of the complete survey and the data is provided in the **Supplementary Materials**.

SURVEY RESULTS

As the sample is based on the subjective view of representatives of the firm, it is important to consider the capability of the respondent to form a well-founded opinion on the statements. Therefore, the respondents have been asked to self-assess their knowledge on the impact of regulatory policies on the company. The majority (72.8%) of the respondents agree or strongly agree with the statement of having a good overview on the impact of regulatory policies on their company. Only four (12.1%) of the respondents disagree with this statement. This gives confidence for a high validity of the answers on the core measurements of the survey. Furthermore, the importance of the CRISPR-Cas technology for the companies responding is of interest. About 45% of the respondents agree or strongly agree with the statement "*The use of CRISPR-Cas technology plays an important role within the development of the products of our company*." In general, the results show no clear tendency in the current importance of use within the companies across the different seed sectors. Also, no significant differences were found when testing on differences across company sizes.

The main results of the survey are provided in **Figure 1**, showing the average scores, differentiated by seed sector in **Figure 1A** and by company size in **Figure 1B**.

Figure 1 shows the perception of negative effects of the ruling on investments and competitiveness. Micro-sized companies expect significantly milder effects on competition than larger-sized companies. The relatively technology-intensive sector of vegetable seeds development (Kokcis et al., 2013) expects the strongest negative effects on competitiveness and investments in CRISPR-Cas applications. Companies in the relatively technology-extensive seed-potato development have diverse expectations (Q6). While they most strongly believe regulatory costs outweigh the benefits of CRISPR-Cas (b), on average they disagree that the ruling will negatively affect competitiveness. This contrasts with expectations of experts in the field (Van 't Hoog, 2019). CRISPR-Cas has especially high potential in speeding up seed-potato development times (Andersson et al., 2018), but breeding companies still expect the bureaucratic hurdle to be too costly. For the potato production in particular this is disappointing as CRISPR-Cas applications are expected to control major diseases that would allow to substantially reduce fungicide use with related benefits for the environment such as reduced environmental and emission of greenhouse gases.

In the survey, Q8 measures the effect of the Court of Justice of the European Union (CJEU) ruling on investments in CRISPR-Cas technology among Dutch plant breeding companies. The

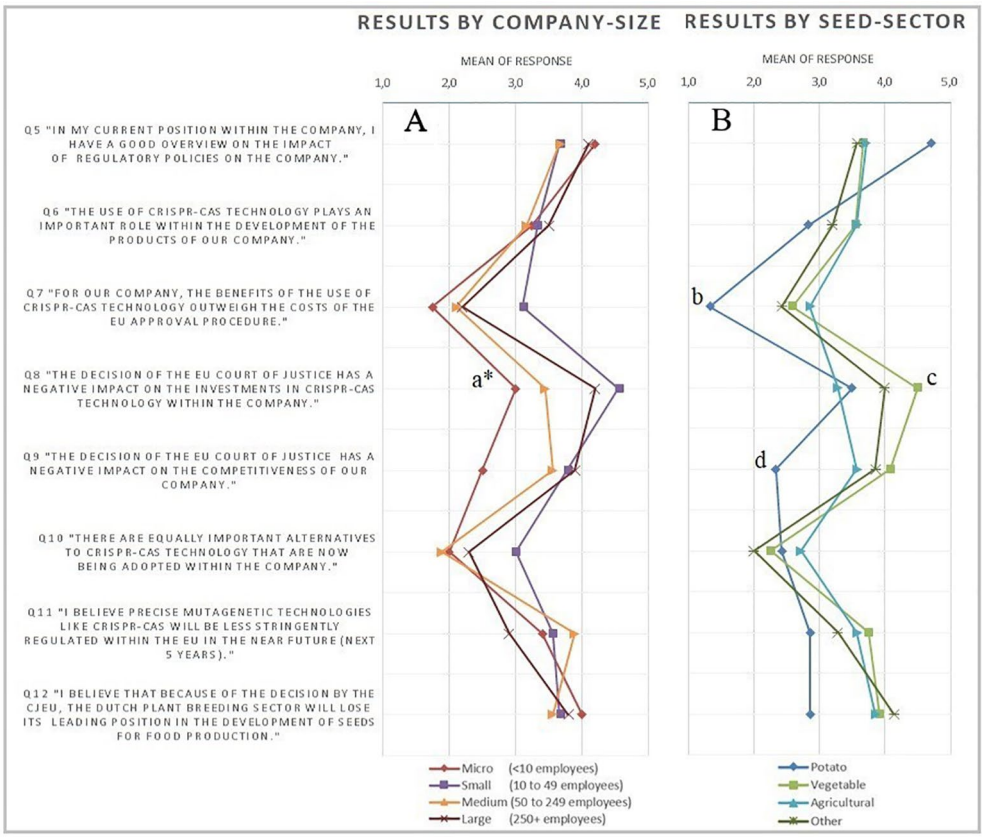

FIGURE 1 | Overview of average results of the survey statements on a five-point Likert-scale, excluding *not relevant (0)* responses ranging from (1) *strongly disagree* to (5) *strongly agree*. Graph panel **(A)** gives the results differentiated by company size, whereas panel **(B)** differentiates the results on seed sector. Statistical results graph panel **(A)**: a* = two-sided significant difference micro from rest ($P < 0.05$) and two-sided significant different distributions among all groups ($P < 0.05$). Statistical results graph panel **(B)**: b = two-sided significant difference potato from all ($P < 0.05$). c = two-sided significant difference vegetable from all ($P < 0.05$). d = two-sided significant different potato from all ($P < 0.05$).

vast majority of the respondents *agree* or *strongly agree* (30.3% and 39.4%, respectively) with the statement in Q8: "*The decision of the EU Court of Justice has a negative impact on the investments in CRISPR-Cas technology within the company*." There appears to be a strong negative effect of the decision of the CJEU on the investments in CRISPR-Cas technology. Looking at **Figure 1A**, the mean responses to statement Q8 appear to differ across company size. The micro- and small-sized companies agree the most on average and experience the least negative impact on investments. The Mann-Whitney U test statistically confirms this difference. The two-tailed (exact) significance is 0.013, which shows that micro-sized companies agree significantly less with the proposed statement in Q8. This is not surprising, as it is intuitively less likely for micro-sized companies to be able to invest in CRISPR-Cas technology anyway. The differentiation in the responses among company sizes is confirmed by the results of the corresponding Kruskal-Wallis test (see **Supplementary Material** for details). Looking at the differences in responses across sectors, mainly the vegetable sector indicates strong negative effects on investments in CRISPR-Cas because of the CJEU ruling. The vegetable sector appeared to agree significantly more with statement Q8 than companies in other sectors. This result has been denoted with letter c in **Figure 1B**.

The third hypothesized effect of the CJEU judgment relates to the comparative disadvantage that plant breeding companies in the Dutch plant breeding sector may be confronted with. This hypothesis was primarily tested by the statement Q9: "*The decision of the EU Court of Justice has a negative impact on the competitiveness of our company*." A majority of 60.6% of the respondents agreed or strongly agreed with this statement, whereas 24.2% disagreed. Testing any differences between company size and the (negative) effects on competition by means of a Kruskal-Wallis test, provides no significant differences. However, the boxplot diagram in the **Supplementary Material** shows a large difference between the modus of the results on statement Q9 of micro-sized companies compared to other-sized companies, while the Mann-Whitney U test does not confirm significant differences and the result therefore needs to be regarded with care.

Nevertheless, the different effect in competitiveness for the micro-sized companies as compared to larger sized companies

might, as suggested by one respondent, be due to the initial accessibility of CRISPR-Cas technique. Smaller, less capital-intensive companies are expected to have lower accessibility to this technique. Therefore, these companies might enjoy some benefit from the ruling of the CJEU, as it equalizes the playing field in terms of use of technology. In the additional comments, a respondent from a micro-sized (<10 employees) remarked: "*We have no possibilities to use these new techniques and therefore can profit slightly from the EU ban on these techniques*." This level playing field has also been pointed out by an EU market-oriented, large (>250 employees) company as well. One respondent commented for example: "*Only a level playing field in the EU is crucial. End customers will get the products they want. If that is food without mutations, we're fine with that*." This would, however, only be true for companies who compete within the EU-market. For EU-based companies who primarily compete on non-EU markets, the limiting factors of the CJEU ruling might lead to larger negative effects in competitiveness. Note that two of the three respondents who indicated that they are moving their research outside the EU, had a non-EU main market. This relation between main-market and (negative) effect on competitiveness could, however, not be confirmed statistically. Based on the Kruskal-Wallis test, no significant difference between the effects on competitiveness across the main market (two-sided asymptotic sig.: 0.170) could be seen. Also, no significant result was found when differentiating between companies with main market within the EU or non-EU (2-sided asymptotic sig, 0.865). Although the latter result was likely to have low significance due to the small number (N = 5) of respondents having a non-EU main market. Besides the strong tendency toward agreement with the statement in results of Q9, three respondents specifically expressed their concerns about the competitiveness for the EU. Most striking is that the companies in the potato sector on average disagree with the statement Q9, and therefore differ from all other sectors. This can also be statistically confirmed by a Mann-Whitney U test. Further analysis among the company characteristics shows that, with one exemption (Africa), all companies in the potato sector appeared to have their main market within the EU. Moreover, the two respondents who pointed out the importance of a level-playing field (over the importance of the use of CRISPR-Cas), were both in the potato sector.

Besides testing the hypothesized negative effects of the CJEU Ruling, the results of the survey allow insights in two more factors that are related to the impact of the hypothesized effects of the ruling of the CJEU. First of all, the effects of the decision depend on the existence of equally important alternatives. When the substitutability of CRISPR-Cas technique is high, any limiting factors of the EU GMO procedure might be diminished. The response to the statement (Q10): "*There are equally important alternatives to CRISPR-Cas technology that are now being adopted within the company*," indicates that the substitutability of CRISPR-Cas appears to be rather low. Only 15.2% of the respondents agreed on having equally important technologies adopted within the company. Especially *in vitro* labs and companies who operate in multiple sectors (including operations as *in vitro* lab) appear to disagree with statement Q10.

Surprisingly, there appears to be a relatively positive attitude of the respondents toward the prospects of the strictness of the EU legislation around mutagenesis-based NPBTs. A majority of 60.6% of the respondents agreed to some degree with the statement in Q11: "*I believe precise mutagenetic technologies like CRISPR-Cas will be less stringently regulated within the EU in the near future (next 5 years)*." When looking at the differences in company sizes (**Figure 1A**), large companies appear to have a relative more pessimistic view, compared to smaller-sized companies. However, no significant differences were found. Among the seed sectors (**Figure 1B**), companies operating in the potato sector are relatively pessimistic, as compared to the other sectors. However, also no significant difference was found.

This general positivism about the development of legislation in the near future (within the next 5 years), is somewhat contrary to the pessimism when asking about the position of the Dutch plant breeding sector as a world leader in the development of seeds for food production. The majority of 63.6% agreed with the statement (Q12) that the Dutch plant breeding sector will lose its leading position in the development of seeds for food production. There seems to be a strong consensus independent of company size (**Figure 1A**). The same applies when differentiating the results by seed sector (**Figure 1B**), although companies in the potato sector appear to be relatively less pessimistic.

DISCUSSION AND CONCLUSIONS

The decision of the CJEU currently places plants produced by NPBTs under the regulations for GMOs. This includes approval and marketing costs, and may result in disincentives for investment in NPBTs in particular in the EU. The survey of Dutch plant breeding companies largely confirms this intuition. The survey also shows that companies with markets outside the EU intend to reallocate their research. Companies that mainly serve the European market and are smaller in size expect their competitiveness to be less affected by the ruling. Nevertheless, the companies agree that the decision will have negative implications for the competitiveness of the Dutch plant breeding sector. Surprisingly, the companies are very optimistic that mutagenetic plant breeding technologies like CRISPR-Cas will be less strongly regulated in the near future.

There is some support for this optimism. A number of stakeholder groups have urged the European Commission to update the approval process for GMOs. A citizens initiative launched by students (https://eci.ec.europa.eu/011/public/#/screen/home) asks for the development of a list of plant breeding technologies that will be exempted from the Directive 2001/18 and would not be considered as GMOs. This is a sensible approach, as it would also avoid the need for labeling products and related problems derived from plants developed by exempted NPBTs. The process for changing the Directive 2001/18 will be difficult. EU member states hold deeply entrenched and diverging views on GMOs (Smart et al., 2015), and finding a qualified majority for

a change will remain a challenge for the European Commission. The results of the survey presented and the results on the patent landscape for CRISPR illustrate the importance and urgency for a change if the EU does not want to fall any further behind in the development and use of the technology. They also suggest negative implications for African development and adaptation to climate change (Wesseler et al., 2017).

Regulating NPBTs similar to "conventional" breeding technologies does not imply that food products will not be regulated. In the EU, food products will still be regulated under the EU food law (Purnhagen, 2019). The same can be observed for other countries (Eriksson et al., 2019). If NPBTs do not fall under the GMO regulation, labeling for food products will be simplified and it reduces costs. A voluntary market for negative labeling in the form of "does not contain…" may emerge similarly to what has been observed in the case of GMOs in the US and the EU (e.g., Castellari et al., 2018; Venus et al., 2018). The advantage of such a labeling scheme is that it is a market-driven response to a demand among some consumers, and similar to products sold under an organic label. Companies participating in such a labeling scheme do this at their own risk and can even differentiate their products according to the labeling schemes.

AUTHOR CONTRIBUTIONS

JW wrote major parts of the contribution, supervised the survey, and finalized the contribution. HP conducted the survey and wrote major parts of the survey results. DZ contributed to the section on the economics of NPBTs and the *Introduction* and *Discussion and Conclusions* sections and reviewed the complete contribution.

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REFERENCES

Andersson, M., Turesson, H., Olsson, N., Fält, A.-S., Ohlsson, P., Gonzalez, M. N., et al. (2018). Genome editing in potato *via* CRISPR-Cas9 ribonucleoprotein delivery. *Physiol. Plant* 164, 5. doi: 10.1111/ppl.12731

Backus, G., Berkhout, P., Eaton, D., de Kleijn, T., van Mil, E., Roza, P., et al. (2009). *EU policy on GMOs: a quick scan of the economic consequences* (The Hague: LEI Wageningen UR).

Beckmann, V., Soregaroli, C., and Wesseler, J. (2010). Ex-ante regulation and ex-post liability under uncertainty and irreversibility: governing the coexistence of GM Crops. *Economics: E-Journal* 4, 2010–2019. doi: 10.5018/economics-ejournal.ja.2010-9

Burns, A., and Bush, R. (2008). *Basic Marketing Research* (New Jersey: Pearson Education).

Callaway, E. (2018). CRISPR plants now subject to tough GM laws in European Union. *Nature* 560 (7716), 16. doi: 10.1038/d41586-018-05814-6

Castellari, E., Soregaroli, C., Venus, T. J., and Wesseler, J. (2018). Food processor and retailer non-GMO standards in the US and EU and the driving role of regulations. *Food Policy* 78, 26–37. doi: 10.1016/j.foodpol.2018.02.010

Coase, R. (1960). The problem of social cost. *J. Law Econ.* 3 (1), 1–44.

Eriksson, D., Kershen, D., Nepomuceno, A., Pogson, B., Prieto, H., et al. (2019). A comparison of the EU regulatory approach to directed mutagenesis with that of other jurisdictions, consequences for international trade and potential steps forward. *New Phytol.* 222 (4), 1673–1684. doi: 10.1111/nph.15627

European Commission. (2007). Economic impact of unapproved GMOs on EU feed imports and livestock production. European commission directorate-general for agriculture and rural development, brussels.

Eurostat. (2018). https://ec.europa.eu/eurostat/tgm/refreshTableAction.do?tab=table&plugin=1&pcode=tag00025&language=en. Utilized Agricultural Area by Categories in thousands of ha. Retrieved 30/01/2018.

Government of the Netherlands. (2017). *The Netherlands, your partner in quality seed* (The Hague: Ministry of Economic Affairs).

James, V. (2017). *Global Status of Commercialized Biotech/GM Crops in 2017: Biotech Crop Adoption Surges as Economic Benefits Accumulate in 22 Years* (Ithaca, NY). The International Service for the Acquisition of Agribiotech Applications (ISAAA).

Jin, Y., Drabik, D., Heerink, N., and Wesseler, J. (2019). Getting an imported GM crop approved in China. *Trends Biotechnol.* 37 (6), 566–569. doi: 10. 1016/j.tibtech.2019.02.004

Kalaitzandonakes, N., Alston, J., and Bradford, K. (2007). Compliance costs for regulatory approval of new biotech crops. *Nat. Biotech.* 25 (5), 509–511. doi: 10.1038/nbt0507-509

Kokcis, V., Weda, J., and Van der Noll, R. (2013). *Concurrentie in de kiem: Mededinging in de Nederlandse veredelingssector* (SEO-rapport; Nr. 2013-11 Amsterdam: SEO Economisch Onderzoek).

Kolstad, C. D., Uhlen, T. S., and Johnson, G. V. (1990). Ex post liability for harm vs. Ex ante safety regulation: substitutes or complements? *Am. Econ. Rev.* 80 (4), 888–901.

Kuntz, M. (2012). Destruction of public and governmental experiments of GMO in Europe. *GM Crops Food* 3 (4), 258–264. doi: 10.4161/gmcr.21231

Martin-Laffon, J., Kuntz, M., and Ricroch, A. E. (2019). Worldwide CRISPR patent landscape shows strong geographical biases. *Nat. Biotech.* 37 (6), 613–620. doi: 10.1038/s41587-019-0138-7

Purnhagen, K., Kok, E., Kleter, G., Schebesta, H., Visser, R. G. F., and Wesseler, J. (2018). EU court casts new plant breeding techniques into regulatory limbo. *Nat. Biotech.* 36, 799. doi: 10.1038/nbt.4251

Purnhagen, K. (2019). How to manage the Union's diversity: the regulation of new plant breeding technologies in *Confédération paysanne and Others. Common Market Law Rev.* 56, 1379–1396.

Purnhagen, K., and Wesseler, J. (2019) Maximum vs. Minimum Harmonization: What to expect from the institutional and legal battles in the EU on Gene editing technologies? *Pest Manag. Sci.* 75, 2310–2315. doi: 10.1002/ps.5367

Shavell, S. (1984). A model of the optimal use of liability and safety regulation. *RAND J. Econ.* 15 (2), 271–280. doi: 10.2307/2555680

Shleifer, A. (2010). "Efficient Regulation," in *Regulation vs. Litigation: Perspectives from Economics and Law*. Eds. D. Kessler (Chicago: University of Chicago Press), 27–43.

Smart, R., Blum, M., and Wesseler, J. (2015). EU member states' voting for authorizing genetically engineered crops: a regulatory gridlock. *Ger. J. Agr. Econ.* 64 (4), 244–262.

Smart, R., Blum, M., and Wesseler, J. (2017). Trends in genetically engineered crops' approval times in the United States and the European Union. *J. Agr. Econ.* 68 (1), 182–198. doi: 10.1111/1477-9552.12171

Smyth, S., Kerr, W., and Phillips, P. (2017). *Biotechnology Regulation and Trade* (New York: Springer). doi: 10.1007/s00299-016-1990-2

Sprink, T., Eriksson, D., Schiemann, J., and Hartung, F. (2016). Regulatory hurdles for genome editing: process- vs. product-based approaches in different regulatory contexts. *Plant Cell Rep.* 35, 1493–1506.

Sullivan, G. M., and Artino Jr, A. R. (2013). Analyzing and interpreting data from likert-type scales. *J. Grad. Med. Edu.* 5 (4), 541–542. doi: 10.4300/JGME-5-4-18

Van 't Hoog, A. (2019). *Ernst van den Ende on CRISPR-Cas*. *Wageningen World* 1, 28–33. http://edepot.wur.nl/472607

Venus, T. J., Drabik, D., and Wesseler, J. (2018). The role of a German multi-stakeholder standard for livestock products derived from non-GMO feed. *Food Policy* 78, 58– 67. doi: 10.1016/j.foodpol.2018.02.009

Wesseler, J., and von Braun, J. (2017). Measuring the bioeconomy: economics and policies. annual review of resource economics. *Annu. Rev. Resour. Econ.* 9, 17.1–17.24. doi: 10.1146/annurev-resource-100516-053701

Wesseler, J., Smart, R., Thomson, J., and Zilberman, D. (2017). Foregone benefits of important food crop improvements in Sub-Saharan Africa. *PloS One* 12 (7), e0181353. doi: 10.1371/journal.pone.0181353

Zaidi, S. S., Vanderschuren, H., Qaim, M., Mahfouz, M. M., Kohli, A., Mansoor, S., et al. (2019). New plant breeding technologies for food security. *Science* 363 (6434), 1390– 1391. doi: 10.1126/science.aav6316

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POLICY AND PRACTICE REVIEWS
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Genebank Operation in the Arena of Access and Benefit-Sharing Policies

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Since the 1990s, the exchange of genetic resources has been increasingly regulated. The Convention on Biological Diversity (CBD), the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA) and the Nagoya Protocol recognize that countries have sovereign rights over their genetic resources and provide a framework for domestic legislations on Access and Benefit-Sharing (ABS). However, within the rules of these international agreements, countries can follow their own interpretations and establish their own rules and regulations, resulting in restricted access to genetic resources and limited benefit-sharing, effects that are contrary to the objectives of these agreements. Although the ITPGRFA's Multilateral System of Access and Benefit-Sharing provides opportunities for easier access to plant genetic resources for food and agriculture (PGRFA), plant genebanks face increasing complexity in their operation. Adding material to genebank collections has become more difficult, not only because collecting missions need to be negotiated with national and local authorities, but also because acquiring material from other collections is only possible if the origin of the material is properly documented and is done in compliance with regulations. Genebanks may only provide access to their own collections if the material that is to be released is distributed in compliance with a) the conditions under which the material was received and b) the national laws of the country where the genebank is located. The only way genebanks can deal with this new complexity, apart from ceasing to add or distribute material, is by setting up proper procedures to document the origin of every accession and the conditions for their use and further distribution. To prevent a further decrease in access to PGRFA, complexity must be fought. Applying the ITPGRFA's Standard Material Transfer Agreement (SMTA) only, even for material that does not fall under the ITPGRFA, would simplify matters. The scope of the ITPGRFA could be expanded to include all crops. Furthermore, certain ambiguities (e.g. regarding *in situ* material and wild species) could be resolved. Finally, compliance with the ITPGRFA should be improved and better monitored.

Keywords: genetic diversity, conservation, genebanks, Access and Benefit-Sharing (ABS), Convention on Biological Diversity (CBD), International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA), Nagoya Protocol

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INTRODUCTION

Plant genetic resources (PGR) include cultivated varieties, obsolete varieties, landraces, wild species (including crop wild relatives), breeders' lines, research populations and mutants. Only a small proportion of all the available PGR are used, and humans depend on a very limited number of crops, in particular wheat, rice and maize, for the largest part of their caloric intake (McCouch et al, 2013; Khoury et al., 2014). The development and expanding cultivation of modern crop cultivars has led to decreased genetic diversity within crops (Langridge et al, 2006; Feuillet et al, 2008; Rufo et al., 2019). This loss of genetic diversity could make adaptation of crops to changing environmental conditions more difficult. Increased temperatures and changing rainfall patterns will cause geographic shifts in suitable cropping areas, and currently well-adapted crops or cultivars may become less adapted or even unsuitable for cultivation. Diversity is needed for crossing and selection, and diversity between and within crops (e.g. by using landraces and crop wild relatives in crop breeding programs) will need to be exploited in order to respond to climate change and to meet future food security challenges (Jump et al., 2009; Ramirez-Villegas et al., 2013; Lopes et al., 2015; Dempewolf et al., 2017; Zhang et al., 2017).

With regard to the conservation of PGR diversity, *in situ* and *ex situ* conservation can be distinguished. *Ex situ* conservation is defined as: "the conservation of components of biological diversity outside their natural habitats", and *in situ* conservation as: "the conservation of ecosystems and natural habitats and the maintenance and recovery of viable populations of species in their natural surroundings and, in the case of domesticated or cultivated species, in the surroundings where they have developed their distinctive properties" (UNEP, 1992). In *ex situ* conservation, the diversity in stored material is fixed because the material is not subject to further natural selection or selection by farmers. (Obviously, while every regeneration of the material will result in slight changes in the genetic composition, maintaining the 'genetic integrity' of the accessions is the goal of *ex situ* conservation.) *In situ* conservation, on the other hand, is more dynamic, but is threatened by climate change and the resulting genetic erosion that can be expected to occur (e.g. Peñuelas et al, 2018). Therefore, the two types of conservation are viewed as complementary.

Genebanks conserve PGR under *ex situ* conditions, make them available for current use and keep them available for future use. As PGR diversity is the foundation of food security and climate resilience, genebanks play an important role in addressing the effects of climate change and other challenges to food security (Pellegrini and Balatti, 2016; Fu, 2017; Westengen et al., 2018). While genebanks previously catered above all to the demands of plant breeders, they have become more involved in long-term conservation and the distribution of PGR material to a wider range of users (Westengen et al., 2018). Some genebanks, such as the Centre for Genetic Resources, the Netherlands (CGN), have evolved into genetic resource centers. They carry out not only *ex situ* conservation but also *in situ* conservation as well as providing services to support PGR users in finding, selecting, obtaining and using PGR.

Users of PGR from genebanks often look for specific traits, such as drought tolerance, resistance to diseases or pests, yield potential, or levels of nutrients or other compounds, e.g. for use in a breeding program. They may also seek diversity for one or more traits for use in a scientific study of a particular trait. Genebanks or plant genetic resources centers help the user to identify the most suitable material and obtain it. Because of ease of access, the primary source of this material often is the collection of the national genebank, followed by other genebanks or *ex situ* sources, and finally *in situ* sources, including natural habitats for crop wild relatives and land of farmers or hobby growers for cultivated material.

However, since the 1990s, obtaining PGR for inclusion in genebanks and further distribution to breeders and other users has become increasingly difficult. Awareness of the actual or potential value of PGR has grown, and as a result an increasing number of countries are asserting their rights to genetic resources. The concept of Access and Benefit Sharing (ABS) was introduced, with ABS being defined as the regulation of access to and utilization of genetic resources and the sharing of the benefits arising from this utilization among users and providers. International ABS agreements were negotiated establishing that states can exercise rights over their genetic resources. This awareness and the resulting agreements have translated into well-structured regulation of access to PGR through domestic legislation in a number of countries. In other countries, however, it has resulted in confusion regarding access to PGR pending the legislative process, or confusion because of the complexity of the regulations.

This article describes the main international ABS agreements concerning PGR (*International Access and Benefit-Sharing Agreements Relevant for PGR*), the implications of these agreements (*Implications*) and the ways genebanks cope with these implications (*How Genebanks Cope*). In the final section (*Recommendations and Conclusions*) the authors outline some recommendations and conclusions.

INTERNATIONAL ACCESS AND BENEFIT-SHARING AGREEMENTS RELEVANT FOR PGR

The Convention on Biological Diversity (CBD)

The three objectives of the Convention on Biological Diversity (CBD, www.cbd.int/convention/), which came into force on 29 December 1993, are the conservation of biological diversity, the sustainable use of its components, and the fair and equitable sharing of the benefits arising from the utilization of genetic resources (UNEP, 1992). In the text of the CBD, genetic resources are defined as: "genetic material of actual or potential value", while genetic material is defined as: "any material of plant, animal, microbial or other origin containing functional units of heredity" (UNEP, 1992).

Prior to the CBD, PGR were generally seen as a common heritage of mankind; PGR were usually freely collected, used, and

transferred to other countries. The CBD, however, established that states can exercise control over the genetic resources in their territories. According to the CBD, prior informed consent of the party providing the resources is needed for access to genetic resources (unless that party has decided otherwise) and use and benefit-sharing must be done according to mutually agreed terms.

Although the CBD is primarily focused on wild biodiversity, it also affects the exchange of plant genetic resources for food and agriculture (PGRFA). The special role of PGRFA was recognized at the Conference for the Adoption of the Agreed Text of the CBD, held in Nairobi in 1992, when a resolution was adopted stating that solutions were to be sought for matters concerning PGR. This would in due time result in the establishment of the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA).

The International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA)

To address PGRFA in the post-CBD era, the FAO drafted and adopted the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA, www.fao.org/plant-treaty), which came into force on 29 June 2004 (FAO, 2002). The objectives of the ITPGRFA are very similar to those of the CBD but focus on PGRFA: the conservation and sustainable use of PGRFA and the sharing of the benefits arising from their use (FAO, 2002). PGRFA are defined as: "any genetic material of plant origin of actual or potential value for food and agriculture" (FAO, 2002). The ITPGRFA confirms the sovereign rights of countries over their genetic resources but aims to facilitate the exchange of PGRFA by the establishment of a Multilateral System of Access and Benefit-Sharing (MLS) in which PGRFA are exchanged under a Standard Material Transfer Agreement (SMTA), instead of under the prior informed consent and mutually agreed terms prescribed by the CBD.

The MLS is a global pool of PGRFA, meant to facilitate access to these PGRFA as well as to achieve fair and equitable sharing of the benefits arising from their utilization. PGRFA may be added to this pool by countries and the institutions under their control, by natural and legal persons in the contracting parties and by international institutes (Manzella, 2013). The MLS does not extend to all PGRFA but covers a set of 35 food crops and 29 forages, which are listed in Annex I of the ITPGRFA. The selection of this set of crops and forages was based on criteria of food security and interdependence and was a negotiated compromise between countries favoring the inclusion of all PGRFA and countries favoring the inclusion of only a limited number of crops (Visser, 2013). According to Article 11 of the ITPGRFA, the MLS is to include all PGRFA of the food crops and forages listed in Annex I that are "under the management and control of the Contracting Parties and in the public domain" (FAO, 2002). PGRFA that belong to the food crops and forages listed in Annex I but do not fulfil the other conditions are not automatically included in the MLS but can be included on a voluntary basis by natural and legal persons holding these PGRFA. Access to materials in the MLS under the SMTA is granted only for their use in research, breeding and training for food and agriculture; other uses are explicitly excluded (FAO, 2002).

With regard to benefit sharing, the Contracting Parties to the ITPGRFA recognize that facilitated access itself is an important benefit, but also underline the importance of other forms of benefit sharing, such as the exchange of information, technology transfer, capacity building, and the sharing of commercial benefits. If material received under an SMTA is used to create PGRFA that are not freely available for research and breeding by others, the recipients must pay 0.77% of the sales of those PGRFA (or 0.5% of all sales of PGRFA belonging to the same crop) to an international benefit-sharing fund (www.fao.org/plant-treaty/areas-of-work/benefit-sharing-fund), which is used to support conservation and sustainable utilization of PGRFA. While information on the projects funded is available on the website, other information, e.g. on financial contributions, is missing.

The Contracting Parties to the ITPGRFA undertake to include in the MLS those PGR of the crops and forages in Annex I that are in the public domain and under their management. However, even if material is not part of the MLS, providers of PGR can distribute their material under the SMTA. The CGIAR centers make more than 750,000 accessions available under the MLS (FAO, 2019).

The Nagoya Protocol

The "Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity" (UNEP, 2011, www.cbd.int/abs) entered into force on 12 October 2014. The Nagoya Protocol is a supplement to the CBD and is intended to improve the implementation of the benefit-sharing provisions of the CBD. Its objective is similar to the third objective of the CBD: the fair and equitable sharing of the benefits arising from the utilization of genetic resources. An Annex gives a long list of possible benefits (monetary and non-monetary) that can be shared.

The Nagoya Protocol not only applies to genetic resources as defined by the CBD, but also contains provisions regarding traditional knowledge associated with genetic resources. It defines the utilization of genetic resources as: "research and development on the genetic and/or biochemical composition of genetic resources, including through the application of biotechnology as defined in Article 2 of the Convention". A major element of the Protocol is that, when genetic resources are used in their territories, Parties must monitor compliance with the domestic ABS rules of provider countries. In addition, Parties to the Protocol must provide rules and procedures for clear and fair access. Each Party must designate a national focal point, responsible for making information available, and a competent national authority, responsible for granting access. An Access and Benefit-Sharing Clearing-House (https://absch.cbd.int/) was established as a means of sharing information related to ABS, including contact details of national focal points and competent national authorities, legislative, administrative and policy measures, and issued permits.

With regard to the relationship between the Protocol and other international agreements, Article 4 states that the Nagoya Protocol is not applicable to genetic resources which are covered by another, specialized international ABS instrument. However, as of November 2019, discussions on the criteria for identifying specialized international ABS instruments and on processes for their recognition had not been concluded, and no specialized instruments have yet been recognized officially under the framework of the Nagoya Protocol. In practice, the ITPGRFA is considered by many countries to be such an instrument, implying that for these countries material exchanges covered by the ITPGRFA are not subject to the rules of the Nagoya Protocol.

More recently, discussion has arisen as to whether digital sequence information (DSI) related to genetic resources should also fall under the international ABS agreements. In general, there is consensus that access to and use of DSI is extremely important for conservation and sustainable development. However, views diverge on whether access to DSI and the sharing of benefits from its use are currently fair and equitable. Countries have different opinions on whether and how access to DSI and benefit-sharing from its utilization should be regulated, and discussions are taking place under the framework of the international agreements. In the meantime, some countries have included DSI in their domestic PGR access legislation.

IMPLICATIONS

After the CBD had come into force (1993), domestic ABS legislation was established in various countries, including the Philippines (1995), Costa Rica (1998) and Brazil (2001). Bilateral agreements between providers and recipients of PGR became the rule for gaining access to them (Carrizosa et al., 2004). However, each country was allowed to have its own interpretations and make its own procedures, which resulted in a complex situation, also due to the uncertainty on how to make access procedures, the costs, and the sometimes insufficient capacity of countries to do this properly. This complex situation sometimes discouraged potential users from seeking access to genetic resources. So, while domestic access and benefit-sharing policies were intended to support, rather than hinder, the sharing of PGRFA (Wynberg et al., 2012), this was often not the case. Adverse effects of CBD-based domestic ABS regulations on biodiversity research and international collaboration have been reported by various authors (Jinnah and Jungcurt, 2009; Neumann et al., 2018; Prathapan et al., 2018).

With regard to access to PGR, the ITPGRFA has been more effective than the CBD, even though not all PGR are incorporated in the MLS, and not all PGR in the MLS are easily available. As of mid-July 2019, more than 5.4 million samples had been distributed (of which 5.2 million from Annex I crops) under about 75,000 SMTAs (FAO, 2019). However, most of the MLS transfers (92%) concern distribution from the collections of the CGIAR centers. Many Contracting Parties to the ITPGRFA have not publicly confirmed which PGR materials in their countries are in the MLS, making it hard for potential users to know which PGR are available (Halewood et al., 2013a). Also, there is much ambiguity about the status of PGR not included in *ex situ* collections but occurring under *in situ* conditions. Bjørnstad et al. (2013) tested the extent to which facilitated access was functioning in practice by sending requests for seeds to 121 countries which were Contracting Parties to the ITPGRFA. They received seeds from 44 of these countries, with 54 countries not responding and contacts with the other 23 countries not resulting in obtaining the seeds requested.

Concerning benefit-sharing under the framework of the ITPGRFA, significant non-monetary benefits have been shared through exchanged material, collaborative research, capacity building, information exchange, and knowledge creation. However, the MLS has hardly been able to generate any monetary benefits based on the use of the SMTA. This may be due to the considerable time that elapses between access to PGRFA and the commercialization of products based on these PGRFA. Also, the SMTA only makes benefit-sharing payments mandatory when the further use of improved material (based on material from the MLS) for research and breeding purposes is restricted (usually through patents). In practice, however, users of material from the MLS do not generally restrict access for research and breeding, and therefore are not subject to mandatory sharing of monetary benefits. A third factor is that some important crops, such as coffee, soya bean, sugarcane and tomato are not included in the current MLS. Much research is done on theses crops, which could have generated mandatory benefit-sharing. Consequently, the benefit-sharing fund of the ITPGRFA has mainly been filled by voluntary donor country contributions. The first mandatory payment to the benefit-sharing fund of the ITPGRFA was only made in 2018, when a Dutch plant breeding company (Nunhems, at the time owned by Bayer) paid about USD 120,000 (0.77% of the US sales revenues of seeds of ten vegetable cultivars developed using material obtained under the SMTA from genebanks in Germany and the Netherlands) (www.fao.org/plant-treaty/news/news-detail/en/c/1143273/).

Discussions are presently being held among the Contracting Parties of the ITPGRFA on proposals to create a subscription system for the MLS to assure earlier and more monetary benefit-sharing. In addition, the possibility of extending ITPGRFA's coverage from the food crops and forages currently mentioned in Annex I to include all PGRFA is being discussed.

Because the Nagoya Protocol has only relatively recently entered into force, it is too early to assess its implications for access to and utilization of genetic resources. However, widespread fear exists among users of genetic resources that the Protocol will have negative consequences, which are likely to include high transaction and administrative costs, reduced access to genetic resources, reduced international collaboration and negative impacts on scientific research and public health (Watanabe, 2015; Comizzoli and Holt, 2016; Cressey, 2017; Deplazes-Zemp et al., 2018; Neumann et al., 2018; Ribeiro et al., 2018). Although all countries have national sovereignty over genetic resources, some Parties to the Protocol have opted not to exercise this national sovereignty and not to require prior informed consent and mutually agreed terms for access to their

genetic resources. Other countries, while having developed access legislation, have given PGRFA a special status, with facilitated access.

When genetic resources are utilized in Parties to the Nagoya Protocol, these Parties are obliged under the Protocol to monitor compliance with ABS rules in the provider countries of these genetic resources. In the EU countries, for instance, this obligation is implemented though EU Regulation 511/2014 (the EU ABS Regulation) (European Commission, 2014). The EU ABS Regulation applies to genetic resources accessed on or after 12 October 2014 in a country that at the time of access was a Party to the Nagoya Protocol and had established access measures. To fall under the EU ABS Regulation, these genetic resources must be used in the EU in basic research, applied research and/or development on their genetic and/or biochemical composition (European Commission, 2016). Where the use of genetic resources falls under the EU ABS Regulation, users must perform due diligence to ensure that the genetic resources they utilize were acquired in compliance with the domestic ABS legislation of the provider country.

Although no specialized international ABS instruments have been recognized yet under the overall framework of the Nagoya Protocol, the ITPGRFA has been explicitly recognized as such in the EU ABS Regulation. This means that PGRFA included in the MLS and acquired from Parties to the ITPGRFA do not fall under the EU ABS Regulation. PGRFA transferred under an SMTA from CGIAR centers do not fall under the EU ABS Regulation either. If non-Annex I PGRFA were obtained under an SMTA from a Party to the Nagoya Protocol that has officially declared that non-Annex I PGRFA under its control can also be transferred under an SMTA, the user of these PGRFA has fulfilled the due diligence obligations of the EU ABS Regulation.

HOW GENEBANKS COPE

Genebanks acquire most new PGR either through collecting missions or through answered requests from other collections. Both channels have become more difficult due to increased regulation. Collecting material from *in situ* sources has become very difficult in many countries. Collecting missions need to be negotiated with national and local authorities, but the procedures and responsibilities within provider countries are often unclear and efforts to gain more clarity are often unsuccessful because those responsible do not respond or are not prepared to make decisions. Obtaining material from other collections is only possible if the material is made available from these and if the origin of the material is properly documented and complies with ABS rules.

With regard to the distribution of material from genebanks, access to their collections can only be provided when distribution complies with the conditions under which the material was received and the domestic legislation of the country where the genebank is located. For instance, if a genebank acquires material under the condition that it can only be used for non-commercial purposes, the genebank cannot make this material available for commercial breeding.

Genebanks are therefore faced with more and more complexity in their operation. The only way genebanks can deal with this, apart from stopping acquisition or distribution of material, is by setting up procedures to properly document the origin of every accession and the conditions for its use and further distribution. This information needs to be made available to potential users. Genebanks will also need to use and store Material Transfer Agreements (MTAs) when material is distributed from the genebank to users. As a result, the volume of paperwork required in the material distribution process has increased significantly.

Apart from the increased complexity of genebank management and the associated costs, the decreased access to PGR is also affecting collaboration between genebanks. Genebanks will be less eager to rationalize their own collections by reducing duplication with other genebanks since they cannot be sure of access to other collections in the future. Indeed, countries might see a need to stockpile PGR material to ensure future access to it for their own research organizations and breeders, resulting in redundancies and a further stress on the already limited capacity of the PGR community.

On the positive side, as the large majority of the users of PGR from genebanks are involved in research, breeding and training for food and agriculture, PGR genebanks often can make use of the MLS of the ITPGRFA, which provides opportunities for facilitated access to PGRFA. This facilitated access involves the use of a standardized contract (SMTA) and procedures, instead of the bilateral, case-by-case contracts and procedures arising from the CBD and Nagoya Protocol. Furthermore, the SMTA can also be used for non-MLS material. The European Cooperative Programme for Plant Genetic Resources (ECPGR) stated in 2016 that "It is recommended that all ECPGR member countries, as appropriate and in line with national legislation, use the SMTA for distribution of both Annex I and non-Annex I PGRFA accessions independently of whether material is conserved in *ex situ* collections or held *in situ*." (ECPGR, 2016). Various countries have already declared that PGR under their management and control and in the public domain are made available by them under the SMTA, irrespective of whether these PGR are of a species contained in Annex I of the ITPGRFA.

In the EU, the ABS Regulation that implements the compliance aspects of the Nagoya Protocol applies to the utilization of genetic resources and not to their possession. The Guidance published by the EU explicitly states that activities such as the management of a collection for conservation purposes are not considered to be utilization. However, genebanks typically aim at making genetic resources available for utilization in breeding and other research and development activities. Therefore, it is good practice for genebanks to support users through seeking, keeping and transferring all relevant information, including access permits and contracts. Furthermore, for genebanks to operate legally, acquisition of PGR should be done in line with the access requirements of the provider country.

The Centre for Genetic Resources, the Netherlands (CGN), a genetic resource center managing the Dutch national plant genebank, may serve as a specific example of how genebanks

cope with increased regulation of access to PGR. CGN operates on two principles: follow the rules and be transparent. The aim is that the origin of all PGR in the CGN collection and the legal basis of their acquisition are traceable. CGN distinguishes three categories of PGR germplasm in relation to its legal status (www.wur.nl/en/show/Access-and-beneft-sharing-Status-of-CGN-collections.htm):

1. Genetic resources of crops listed in Annex I of the ITPGRFA and forming part of the MLS. Access to these collections is provided under the SMTA of the ITPGRFA;
2. Genetic resources not listed in Annex I of the ITPGRFA and acquired by CGN before the CBD entered into force. In principle, CGN will provide this germplasm to the user under the SMTA, unless contractual obligations agreed upon during acquisition of the material by CGN require additional conditions;
3. Genetic resources not listed in Annex I of the ITPGRFA and acquired by CGN after the CBD entered into force. These are subject to the national sovereignty of the country of origin. Where possible, CGN provides access to these genetic resources under the SMTA, but where needed, CGN adapts the SMTA to incorporate additional conditions set by the provider country or contractual obligations agreed upon during acquisition of the material by CGN.

The "regular" CGN collection contains about 23,000 accessions of a range of agricultural and horticultural crops. In addition to its regular collection, CGN also offers seed samples from "special collections" that have been developed for a specific purpose targeting specific user groups, such as a collection of 73 re-sequenced tomato lines and a collection of 470 single seed descent (SSD) lines of *Lactuca* spp. CGN's aim is to be able to make its regular PGR collection available in perpetuity, with all material being fully and freely available under SMTA (where it is to be used for research, breeding, or training for food and agriculture purposes), as the use of the SMTA reduces complexity and the free availability reduces transaction costs.

To achieve this, CGN makes all possible efforts to acquire and only include in its collection material that can be distributed in this way. This means that collecting missions are undertaken after signing an agreement in which the Competent National Authority of the country where the collecting takes place agrees with the subsequent distribution of collected material by CGN under the terms and conditions of the SMTA. The modalities are laid down in a Memorandum of Understanding between CGN and the Competent National Authority of the country of collection. The Memorandum of Understanding may cover a single collection mission or various collection missions over an extended period of time, as CGN strives to establish multiyear collaborations with countries. With respect to the benefit-sharing component of the agreements, CGN aims to include a substantial capacity development component. This may, for instance, include participation of representatives of the provider country in international courses on the conservation and use of PGR or the organization of tailor-made PGR courses in the provider country itself by CGN staff.

Unfortunately, not all countries or institutes from which CGN would like to acquire material are willing to allow incorporation of these PGR in the CGN genebank under the conditions of the SMTA. Some countries, for instance, are not comfortable with the associated multilateral character of monetary benefit-sharing and prefer bilateral sharing of monetary benefits instead. In these cases, the material cannot be acquired under the conditions of the SMTA and will thus not be included in the regular CGN collection. Since the material might still be valuable to some users, the possibility of creating a special collection for that material exists, but this is only done in exceptional cases. These special collections with material that can only be distributed under additional conditions are generally maintained on the principle of cost recovery, and access may need to be negotiated (possibly even with the donor of the material).

CGIAR genebanks too have been facing increasing difficulties in their efforts to acquire and conserve PGR in the past decades, for a large part due to ABS issues (Halewood et al., 2013b). The collections of the CGIAR genebanks have been placed in the MLS of the ITPGRFA, which means that the PGR included are available under the SMTA. As such, their activities are mainly governed by the ITPGRFA. However, when these genebanks want to acquire materials that are not included in the MLS, they have to comply with domestic access regulations based on the CBD and the Nagoya Protocol. Guidelines have been developed for the CGIAR genebanks on how to comply (CGIAR Genebank Platform, 2018).

RECOMMENDATIONS AND CONCLUSIONS

Policy developments since the 1990s that were aimed at regulating Access and Benefit-Sharing have so far resulted in reduced access. This is felt by genebanks, which face increasing difficulties in adding material to their collections, either through collecting missions or by obtaining material from other collections. As genebanks play a key role in conserving and making available key resources to address climate change and other challenges to food production and food security, this is an undesirable and possibly even dangerous development. Given climate change and the resulting genetic erosion that can be expected to occur, collecting and subsequent conservation in genebanks are essential for limiting losses of valuable PGR.

The national sovereignty of countries over their genetic resources has been firmly established and genebanks have to comply with the domestic access regulations in the countries where they collect material. As illustrated above, genebanks accept this and are fully committed to comply with domestic ABS measures. They are ready to share benefits, especially through capacity development in the countries where they collect. However, genebanks struggle with the complexity and unclarity of the way this sovereignty is exercised at the domestic and international levels.

To prevent a further decrease in access to PGRFA, this complexity must be fought. Although ABS issues are inherently

complex, the resulting ABS regime should be kept as simple as possible. Acquisition and distribution of germplasm have to stay workable for genebanks as these activities play an important role in assuring the world's food supply in the current times of climate crisis and population growth.

The ITPGRFA and its SMTA could play a key role in reducing complexity. The CBD and the Nagoya Protocol do not prescribe in detail how ABS should be implemented through domestic legislation and leave room for countries to decide for themselves how to exercise their sovereignty over their PGR. Applying the SMTA also to material not contained in Annex I to the ITPGRFA (and thus not in the MLS), would simplify matters. Various countries have already decided to do so for PGR under their management and control and in the public domain.

It should also be made clearer for potential users which PGR of Annex I crops and forages in ITPGRFA countries are available in the MLS. More clarity should be created on the status of *in situ* material in the context of the ITPGRFA. To achieve this, compliance with the ITPGRFA should be improved and better monitored. While the ITPGRFA has 145 member countries, only 54 national reports on the implementation of the ITPGRFA are available on the ITPGRFA website (www.fao.org/plant-treaty/areas-of-work/compliance/compliance-reports/en/). In comparison, for the Nagoya Protocol, which had 120 member countries as of 22 November 2019, 94 national implementation reports were available on the ABS Clearing house website on that date (absch.cbd.int/reports).

Contracting Parties to the ITPGRFA have been discussing expansion of the scope of the MLS of the ITPGRFA from the 64 food crops and forages mentioned in Annex I of the ITPGRFA to include all PGRFA. In addition, they have been considering the idea of creating a subscription system for the MLS to assure earlier and more monetary benefit-sharing. Expansion of the MLS would be a major development in the process of reducing the complexity. As the lack of sharing of monetary benefits from the utilization of materials provided through the MLS has remained an issue affecting the readiness of provider countries to allow access to their PGR through the MLS, the creation of a subscription system may not only result in more benefit-sharing but also in better access. Unfortunately, an agreement on the expansion of the MLS and the creation of a subscription system was not reached during the ITPGRFA Governing Board meeting held in November 2019. This was mainly due to diverging views as to whether access to DSI related to genetic resources from the MLS and benefit-sharing from its utilization should be regulated under the ITPGRFA.

In the end, it is in the interest of all countries that genebanks continue to be able to play their role of conserving and making available the key resources that are needed for meeting the demands of a growing world population in a changing climate.

AUTHOR CONTRIBUTIONS

MB and TH both contributed to the conception and design of the article. MB wrote the first draft of the manuscript, with TH writing additional sections. Both authors contributed to manuscript revision, read and approved the submitted version.

REFERENCES

Bjørnstad, Å., Tekle, S., and Göransson, M. (2013). "Facilitated access" to plant genetic resources: does it work? *Genet. Resour. Crop Evol.* 60 (7), 1959–1965. doi: 10.1007/s10722-013-0029-6

Carrizosa, S., Brush, S. B., Wright, B. D., and McGuire, P. E. (2004). *Accessing Biodiversity and Sharing the Benefits: Lessons from Implementing the Convention on Biological Diversity. IUCN Environmental Policy and Law Paper No 54* [Gland: International Union for Conservation of Nature (IUCN)].

CGIAR Genebank Platform. (2018). *Guidelines on the Nagoya Protocol for CGIAR Research Centers* (Montpellier: CGIAR).

Comizzoli, P., and Holt, W. V. (2016). Implications of the Nagoya Protocol for genome resource banks composed of biomaterials from rare and endangered species. *Reprod. Fertil. Dev.* 28 (8), 1145–1160. doi: 10.1071/RD15429

Cressey, D. (2017). Treaty to stop biopiracy threatens to delay flu vaccines. *Nature* 542 (7640), 148. doi: 10.1038/542148a

Dempewolf, H., Baute, G., Anderson, J., Kilian, B., Smith, C., and Guarino, L. (2017). Past and future use of wild relatives in crop breeding. *Crop Sci.* 57, 1070–1082. doi: 10.2135/cropsci2016.100885

Deplazes-Zemp, A., Abiven, S., Schaber, P., Schaepman, M., and Schaepman-Strub, G. (2018). The Nagoya Protocol could backfire on the Global South. *Nat. Ecol. Evol.* 2, 917–919. doi: 10.1038/s41559-018-0561-z

ECPGR. (2016). *Report of the Fourteenth Steering Committee Meeting, 31 May - 2 June 2016, Višegrad, Bosnia and Herzegovina* [Rome: European Cooperative Programme for Plant Genetic Resources (ECPGR)/Bioversity International].

European Commission. (2014). Regulation (EU) no 511/2014 of the European Parliament and of the Council of 16 April 2014 on compliance measures for users from the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization in the Union. *Off. J. Eur. Union. L.* 150, 59–71.

European Commission. (2016). Guidance document on the scope of application and core obligations of Regulation (EU) No 511/2014 of the European Parliament and of the Council on the compliance measures for users from the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilisation in the Union. *Off. J. Eur. Union. C.* 313, 1–19.

FAO. (2002). *International Treaty on Plant Genetic Resources for Food and Agriculture* [Rome: Food and Agriculture Organization of the United Nations (FAO)].

FAO. (2019). *Report on the Implementation and Operations of the Multilateral System. Eighth Session of the Governing Body, 11-16 November 2019, Rome* [Rome: Food and Agriculture Organization of the United Nations (FAO)].

Feuillet, C., Langridge, P., and Waugh, R. (2008). Cereal breeding takes a walk on the wild side. *Trends Genet.* 24 (1), 24–32. doi: 10.1016/j.tig.2007.11.001

Fu, Y. (2017). The vulnerability of plant genetic resources conserved ex situ. *Crop Sci.* 57, 2314–2328. doi: 10.2135/cropsci2017.010014

Halewood, M., López Noriega, I., and Louafi, S. (2013a). "The global crop commons and access and benefit-sharing laws: examining the limits of policy support for the collective pooling and management of plant genetic resources," in *Crop Genetic Resources as a Global Commons: challenges in international law and governance*. Eds. M. Halewood, I. López Noriega and S. Louafi (Abingdon, UK: Routledge), 1–36.

Halewood, M., Sood, R., Sackville Hamilton, R., Amri, A., Van den Houwe, I., Roux, N., et al. (2013b). "Changing rates of acquisition of plant genetic resources by international genebanks," in *Crop Genetic Resources as a Global Commons: challenges in international law and governance*. Eds. M. Halewood, I. López Noriega and S. Louafi (Abingdon, UK: Routledge), 99–131.

Jinnah, S., and Jungcurt, S. (2009). Could Access Requirements Stifle Your Research? *Science* 323 (5913), 464–465. doi: 10.1126/science.1167234

Jump, A. S., Marchant, R., and Peñuelas, J. (2009). Environmental change and the option value of genetic diversity. *Trends Plant Sci.* 14, 51–58. doi: 10.1016/j.tplants.2008.10.002

Khoury, C. K., Bjorkman, A. D., Dempewolf, H., Ramirez-Villegas, J., Guarino, L., Jarvis, A., et al. (2014). Increasing homogeneity in global food supplies and the implications for food security. *Proc. Natl. Acad. Sci.* 111 (11), 4001–4006. doi: 10.1073/pnas.1313490111

Langridge, P., Paltridge, N., and Fincher, G. (2006). Functional genomics of abiotic stress tolerance in cereals. *Brief Funct. Genomics* 4 (4), 343–354. doi: 10.1093/bfgp/eli005

Lopes, M. S., El-Basyoni, I., Baenziger, P. S., Singh, S., Royo, C., Ozbek, K., et al. (2015). Exploiting genetic diversity from landraces in wheat breeding for adaptation to climate change. *J. Exp. Bot.* 66 (12), 3477–3486. doi: 10.1093/jxb/erv122

Manzella, D. (2013). "The design and mechanics of the multilateral system of access and benefit-sharing," in *Crop Genetic Resources as a Global Commons: challenges in international law and governance*. Eds. M. Halewood, I. López Noriega and S. Louafi [(Abingdon, UK: Routledge], 150–163.

McCouch, S., Baute, G. J., Bradeen, J., Bramel, P., Bretting, P. K., Buckler, E., et al. (2013). Agriculture: Feeding the future. *Nature* 499, 23–24. doi: 10.1038/499023a

Neumann, D., Borisenko, A. V., Coddington, J. A., Häuser, C. L., Butler, C. R., Casino, A., et al. (2018). Global biodiversity research tied up by juridical interpretations of access and benefit sharing. *Org. Divers. Evol.* 18, 1. doi: 10.1007/s13127-017-0347-1

Pellegrini, P. A., and Balatti, G. E. (2016). Noah's arks in the XXI century. *A. Typol. Seed Banks Biodivers. Conserv.* 25, 2753. doi: 10.1007/s10531-016-1201-z

Peñuelas, J., Sardans, J., Filella, I., Estiarte, M. L., Ogaya, J. R., et al. (2018). Assessment of the impacts of climate change on Mediterranean terrestrial ecosystems based on data from field experiments and long-term monitored field gradients in Catalonia. *Environ. Exp. Bot.* 152, 49–59. doi: 10.1016/j.envexpbot.2017.05.012

Prathapan, K. D., Pethiyagoda, R., Bawa, K. S., Raven, P. H., Dharma Rajan, P.and 172 co-signatories from 35 countries (2018). When the cure kills - CBD limits biodiversity research. *Science* 362 (6413), 404–406. doi: 10.1126/science.aat9844

Ramirez-Villegas, J., Jarvis, A., Fujisaka, S., Hanson, J., and Leibing, C. (2013). "Crop and forage genetic resources: international interdependence in the face of climate change," in *Crop Genetic Resources as a Global Commons: challenges in international law and governance*. Eds. M. Halewood, I. López Noriega and S. Louafi (Abingdon, UK: Routledge), 78–98.

Ribeiro, C., dos, S., Koopmans, M. P., and Haringhuizen, G. B. (2018). Threats to timely sharing of pathogen sequence data. *Science* 360 (6396), 1405–1406. doi: 10.1126/science.aau5229

Rufo, R., Alvaro, F., Royo, C., and Soriano, J. M. (2019). From landraces to improved cultivars: assessment of genetic diversity and population structure of Mediterranean wheat using SNP markers. *PloS One* 14 (7), e0219867. doi: 10.1371/journal.pone.0219867

UNEP. (1992). *Convention on Biological Diversity* (Montreal: United Nations Environmental Programme (UNEP), Secretariat of the Convention on Biological Diversity).

UNEP. (2011). *Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity* (Montreal: United Nations Environmental Programme (UNEP), Secretariat of the Convention on Biological Diversity).

Visser, B. (2013). "The moving scope of Annex 1: the list of crops covered under the multilateral system," in *Crop Genetic Resources as a Global Commons: challenges in international law and governance*. Eds. M. Halewood, I. López Noriega and S. Louafi (Abingdon, UK: Routledge), 265–282.

Watanabe, M. E. (2015). The Nagoya Protocol on Access and Benefit Sharing: International treaty poses challenges for biological collections. *BioScience* 65 (6), 543–550. doi: 10.1093/biosci/biv056

Westengen, O. T., Skarbø, K., Mulesa, T. H., and Berg, T. (2018). Access to genes: linkages between genebanks and farmers' seed systems. *Food Sec.* 10, 9. doi: 10.1007/s12571-017-0751-6

Wynberg, R., van Niekerk, J., Williams, R., and Mkhaliphi, L. (2012). *Securing Farmers' Rights and Seed Sovereignty in South Africa* (Durban: Biowatch).

Zhang, H., Mittal, N., Leamy, L. J., Barazani, O., and Song, B. (2017). Back into the wild—Apply untapped genetic diversity of wild relatives for crop improvement. *Evol. Appl.* 10, 5–24. doi: 10.1111/eva.12434

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The Judgment of the CJEU of 25 July 2018 on Mutagenesis: Interpretation and Interim Legislative Proposal

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The Judgment of 25 July 2018 of the Court of Justice of the European Union (CJEU)[1] was optimistically awaited by breeders and supporters of agricultural biotechnology, but shortly after the press release advancing the Judgment, hope turned into frustration. Opinions on how to frame the New Breeding Techniques (NBT) in the context of Directive 2001/18/EC were issued before the Judgment, while proposals to assist the EU legislator to amend the regime driven by the Directive have been also provided afterwards by scientists and institutional bodies around the EU. However, they do not seem to have paid so much attention to the Judgment itself. This paper focuses on the Judgment. It finds out that while the impacts of the Judgment on the NBT might have been slightly overvalued, its potential negative effects on techniques of random mutagenesis and varieties breed through them have been generally underestimated if not absolutely overlooked. The analysis also shows that the Judgment does not preempt the possibility to exempt certain applications of some NBT from the scope of Directive 2001/18/EC,[2] and, in fact, ODM, SDN1, and SDN2 might be, under certain conditions, easily exempted from its scope without the need of a deep legislative revolution nor even the amendment of Directive 2001/18/EC. As regards techniques of random mutagenesis and mutant varieties bred by means of those techniques, until action is taken by Member States (if finally taken), no real limitations upon them are to be feared. However, if Member States start to consider the path opened by the CJEU, then their regulation at an EU level should be readily explored in order to avoid further negative effects on plant breeding as well as on the free movement inside the EU of those varieties and the products thereof.

Keywords: mutagenesis, gene editing, GMO, Directive 2001/18/EC, C-528/16, Court of Justice of the European Union, plant breeding, plant biotechnology

[1] Judgment of 25 July 2018, *Confédération paysanne and Others*, C-528/16, EU:C:2018:583.
[2] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.

INTRODUCTION

After a fairly pro-biotech Opinion of Advocate General Bobek[3] [see, e.g., Purnhagen et al. (2018a; 2018b) and Callaway (2018)], the Judgment of 25 July 2018, *Confédération paysanne and Others*, C-528/16, EU:C:2018:583 of the Court of Justice of the European Union (CJEU) (from now on "the Judgment" or "*Confédération paysanne and Others*") deeply disappointed the scientific community [see, e.g., Callaway (2018) or Urnov et al. (2018)], because it "classifies genome-edited plants as genetically modified organisms (GMOs) and thus subjects them to prohibitive premarket risk evaluations" (Urnov et al., 2018: 800). After the Judgment, scientists [see, e.g., Urnov et al. (2018)], advisory bodies, such as the German Bioeconomy Council [see Bioökonmierat (2018)] and the European Commission's Group of Chief Scientific Advisors [see SAM (2018)], and more recently even the European Commissioner for Health and Food Safety (Michalopoulos, 2019) have urged to review Directive 2001/18/EC in order to overcome the Judgment. However, a deeper analysis of the Judgment and its impact on the EU legal regime on GMO seems to be needed. This paper focuses on the Judgment, aiming to debunk some myths around it and clarify its meaning, and to present a proposal addressed to mitigate its potential negative effects on plant breeding, the EU legal regime on GMO and the internal market.

MATERIALS AND METHODS

The paper is organized in three sections. The section *Interpretation of the Judgment of the CJEU of 25 July 2018* focuses on the interpretation of the Judgment; the section *Leeway to Operate Out of the Scope of Directive 2001/18/EC Post Judgment* analyzes the leeway to operate out of the scope of Directive 2001/18/EC post Judgment by means of a legislative proposal expressly designed with that purpose; and the section *Analysis of the Impact of the Judgment on the Breeding Techniques* focuses on the impact of the Judgment on the legal status of breeding techniques, and assesses the feasibility and potential usefulness of the legislative proposal outlined in the section *Leeway to Operate Out of the Scope of Directive 2001/18/EC Post Judgment*.

In the section *Interpretation of the Judgment of the CJEU of 25 July 2018*, the Judgment is analyzed by means of the application of well-known principles and rules of legal interpretation in the EU and taking leverage on the analysis of the relevant literature on the EU legal regime on GMO [most remarkably Spranger (2015) and Krämer (2015)]. This exercise has been enrichened with the analysis of relevant reactions to the Judgment from the industry, politicians, and scientific scholars (gathered from websites, electronic newspapers, papers, and other electronic sources found through searches on Google, Google Scholar, WoS, or from pgrip.org). Recourse has also been made to the Opinion of Advocate General Bobek and the Decision[4] of the referring French court.

In the section *Leeway to Operate Out of the Scope of Directive 2001/18/EC Post Judgment*, trough legal reasoning and on the basis of the analysis performed in the section *Interpretation of the Judgment of the CJEU of 25 July 2018*, a prospective exercise on the leeway to operate out of the scope of Directive 2001/18/EC post Judgment has been conducted, and a legislative proposal has been outlined.

In the section *Analysis of the Impact of the Judgment on the Breeding Techniques*, legal interpretation is combined with scientific/technical analysis to assess the impact of the Judgment on the legal status of the existent breeding techniques (on the basis of the analysis performed in the section *Interpretation of the Judgment of the CJEU of 25 July 2018* and a nonexhaustive literature review on breeding techniques). The possibility to exempt the breeding techniques assessed in this section by means of the legislative proposal outlined in the section *Leeway to Operate Out of the Scope of Directive 2001/18/EC Post Judgment* has been also evaluated.

RESULTS AND DISCUSSION

Interpretation of the Judgment of the CJEU of 25 July 2018

A "Shocking" Decision

After the press release of the CJEU on its Judgment, "shocked" (Michalopoulos, 2018; Science Media Centre, 2018) and "disappointing" (Callaway, 2018: 16; Science Media Centre, 2018) were likely the words best summarizing the mood of the industry and scientists. Since then, beyond some scarce exceptions in which scholars have shown a greater awareness toward the difficult task of the Court [see, e.g., Leyser (2018) and Purnhagen et al. (2018a)], the Judgment and the EU legal regime on GMO have been the target of a general criticism, not only from the Academia and the industry [see, e.g., Michalopoulos (2018) and Urnov et al. (2018)] but also from within EU institutions [see SAM (2018) and Michalopoulos (2019)]. Indeed, after the positive expectations created by the Opinion of Advocate General Bobek (Callaway, 2018; Michalopoulos, 2018; Purnhagen et al., 2018a; Science Media Centre, 2018; Marks and Livingstone, 2019), the Judgment does not bring good news to plant breeders and the agricultural sector (Michalopoulos, 2018; Purnhagen et al., 2018a; Science Media Centre, 2018; Urnov et al., 2018). However, it needs to be noted that the approach of the Court toward NBT, aligned with "the Applicants [Confédération paysanne and Others] together with the French Government" (Opinion of Advocate General Bobek, para 87), is coherent with the European understanding of the precautionary principle in this field as well as with recital 17 Directive 2001/18/EC [anticipated by legal scholars like Krämer (2015) and Spranger (2015), and noticed

[3] Opinion of Advocate General Bobek delivered on 18 January 2018 on the case C-528/16, *Confédération paysanne and Others*, C-528/16, ECLI:EU:C:2018:20. Cited in the text as the "Opinion of Advocate General Bobek", the "Opinion of the Advocate General", or simply, the "Opinion".

[4] Conseil d'État, 3ème - 8ème chambres réunies, 03/10/2016, *Confederation Paysanne et autres*, No. 388649, FR:CECHR:2016:388649.20161003.

also by Purnhagen et al. (2018a) and Eriksson (2018)]. Certainly, the role of recital 17 Directive 2001/18/EC acknowledged by the Court contradicts the approach of the Advocate General to recital 17 Directive 2001/18/EC based on historical interpretation (*cf.* paras 90 ff of the Opinion of the Advocate General with paras 44, 51, 54 and the conclusion of the Judgment). However, historical interpretation is far from being the usual approach of the CJEU (Rösler, 2012; Scholz and Cunha, 2017; Purnhagen et al. 2018a). That art 3(1) Directive 2001/18/EC is to be interpreted "strictly" (para 41 of the Judgment) was already anticipated by Krämer (2015) and Spranger (2015). Besides, the need to take into account "the context […] and the objectives pursued by the rules of which it is part" (Judgment, para 42) and the principle of narrow interpretation of exemptions (Judgment, para 41), are well known rules of legal interpretation in the EU [see, e.g., Scholz (2012a; 2012b) and Beck (2012)] and was also anticipated by Krämer (2015) and Spranger (2015). In fact, the conclusions and reasoning of the Court were anticipated by Krämer (2015) and Spranger (2015) to a large extent. In the light of the foregoing, the Judgment, at least as regards its conclusions on NBT, can hardly be deemed groundless from a legal perspective nor surprising. From a rational and a scientific perspective though, as manifested by some scholars [see, e.g., Leyser (2018) or Purnhagen et al. (2018a)], the Judgment is just as objectionable as the EU legal regime on GMO.

Directive 2001/18/EC: Recital 17 and art 3(1)

- Recital 17 Directive 2001/18/EC reads as follows: "(17) This Directive should not apply to organisms obtained through certain techniques of genetic modification which have conventionally been used in a number of applications and have a long safety record." This recital is connected with the precautionary principle (Krämer, 2015; Spranger, 2015).
- Art 3(1) Directive 2001/18/EC: "This Directive shall not apply to organisms obtained through the techniques of genetic modification listed in Annex I B."

The precautionary principle

The precautionary principle has its roots in the German law (Andrew and O'Riordan, 2004) and its recognized, although not defined, in art 191 of the Treaty of Functioning of the European Union (TFEU) (European Union, 2016), but it has been developed by the Communication from the Commission on the precautionary principle (Brussels, 2.2.2000 COM(2000) 1 final) (Andrew and O'Riordan, 2004). As understood by the Communication from the Commission, "the precautionary principle which enables a rapid response to be given in the face of a possible danger to human, animal or plant health, or to protect the environment. In particular, where scientific data do not permit a complete evaluation of the risk, recourse to this principle may, for example, be used to stop distribution or order withdrawal from the market of products likely to be hazardous" (European Union, 2016).

Historical interpretation of law

As explained by Scholz and Cunha (2017): "Historical interpretation, in the case of EU law, relies on the historical background, the content of *travaux preparatoires* [preparatory work] or similar materials, which record the legislators' intention and the purpose for which the provision was made."

Regulatory Changes "On the Way"

After the Judgment, the idea of a revision of the EU legal framework on GMO as a reaction to interpretation of the CJEU [see, e.g., Bioökonmierat (2018); Michalopoulos (2019) and Urnov et al. (2018)] gained momentum, resulting in the "Statement by the Group of Chief Scientific Advisors"[5] [see SAM (2018)]. However, in the current European context as regards GMO, defined by Directive (EU) 2015/412,[6] Commission Implementing Decision (EU) 2016/321 of 3 March 2016,[7] and by the Judgment itself, this headlong rush toward a new GMO legal framework does not seem to have much chances of success in the short term [see also Purnhagen et al. (2018b)]. In fact, hastiness might contribute to further intensify polarization of public opinion in Europe on this issue [see, e.g., in this respect Gelinsky and Hilbeck (2018); Noisette (2019) and Antoniou (2019)] "reducing the possibility of breaking deadlock" (Mandel, 2005: 168) in the short to medium term. Furthermore, it also seems to have unintentionally prevented a sober analysis of some aspects of the Judgment that might have relevant implications on plant breeding and agriculture.

The Judgment on "NBT"

The application before the *Conseil d'État* (the French court that referred the questions for preliminary ruling) requested to "revoke Article D. 531-2 of the Environmental Code, transposing Directive 2001/18, which excludes mutagenesis from the definition of techniques giving rise to genetic modification within the meaning of Article L. 531-1 of the code, and ban the cultivation and marketing of herbicide-tolerant rape varieties obtained by mutagenesis" (Judgment, para 20). Therefore, the request was not focused on NBT but on herbicide tolerant crops (Eriksson, 2018; Leyser, 2018) and on mutagenesis (Purnhagen et al., 2018a; 2018b) in a broad sense. Furthermore, as acknowledged by the *Conseil d'État*, "[t]he only herbicide resistant seeds registered in the common catalogue of varieties of agricultural plant species are the result of *in vitro* random mutagenesis. […] no variety of herbicide resistant seed resulting from the directed mutagenesis techniques has yet been included in the common catalogue" (Opinion, para 25). Besides, the Decision of the *Conseil d'État*, the Opinion of Advocate General Bobek, and the Judgment itself have all of them a broader scope than strictly NBT. Even the heading of the press release of the CJEU on the Judgment [see CJEU (2018)] refers to mutagenesis in a broad sense, not only to NBT. In fact, the conclusions of the Court in its Judgment deal more on mutagenesis *lato sensu* and even on the concept of GMO, than on NBT. However, after the Judgment, most of the scientific

[5] "Statement by the Group of Chief Scientific Advisors: A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive."

[6] Directive (EU) 2015/412 of the European Parliament and of the Council of 11 March 2015 amending Directive 2001/18/EC as regards the possibility for the Member States to restrict or prohibit the cultivation of genetically modified organisms (GMOs) in their territory.

[7] Commission Implementing Decision (EU) 2016/321 of 3 March 2016 adjusting the geographical scope of the authorisation for cultivation of genetically modified maize (Zea mays L.) MON 810 (MON-ØØ81Ø-6).

publications [see, e.g., Callaway (2018) and Purnhagen et al. (2018a)] and press publications [see, e.g., The Irish Times (2019); Marks and Livingstone (2019) or Zimmere (2018)] focused mainly on the impacts of the Judgment on NBT, not on mutagenesis in a broad sense. In the end, the Judgment itself has come to be known as the "ruling on new breeding techniques" [see, e.g., Opoku Gakpo (2018) or Devuyst (2018)]. As shown in the following paragraphs, this bias in the interpretation of the Judgment might be involuntarily concealing some relevant potential effects of the Judgment on plant breeding and free trade in the EU that should be known and, where appropriate, adequately addressed.

Varieties Bred Through Traditional Techniques of Random Mutagenesis "Saved From the Purge" of the Court

Due to the shift of attention toward NBT above described, potential implications of the Judgment on traditional techniques of random mutagenesis and varieties thereof have been generally overlooked or misinterpreted [among the very few exceptions see Martin in Science Media Centre (2018), Gelinsky and Hilbeck (2018), CIOPORA (2018), Wanner et al. (2019), or Jorasch (2019)].

The *Conseil d'État*, in its third question referred for a preliminary ruling, asked the CJEU whether "[a]rticles 2 and 3 of [*sic.*] and Annex I B to Directive [2001/18] on the deliberate release into the environment of [GMOs] constitute […] a full harmonization measure prohibiting Member States from subjecting organisms obtained by mutagenesis to all or some of the obligations laid down in the directive or to any other obligation, or do the Member States, when transposing those provisions, have a discretion to define the regime to be applied to organisms obtained by mutagenesis" (para 25 of the Judgment). The Judgment concludes that "[a]rticle 3(1) of Directive 2001/18 […] does not have the effect of denying Member States the option of subjecting such organisms […] to the obligations laid down in that directive or to other obligations" (para 82).

Directive 2001/18/EC: Recital 17 and art 3(1)

- Art 2(2) Directive 2001/18/EC: "(2) "genetically modified organism (GMO)" means an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination;Within the terms of this definition:
  a. genetic modification occurs at least through the use of the techniques listed in Annex I A, part 1;
  b. the techniques listed in Annex I A, part 2, are not considered to result in genetic modification;".
- Annex I B Directive 2001/18/EC:
  "TECHNIQUES REFERRED TO IN ARTICLE 3
  Techniques/methods of genetic modification yielding organisms to be excluded from the 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 techniques/methods listed below are:
  1. mutagenesis,
  2. cell fusion (including protoplast fusion) of plant cells of organisms which can exchange genetic material through traditional breeding methods."

The Court justified its positioning by arguing that "to the extent to which the EU legislature has not regulated those organisms, Member States have the option of defining their legal regime" (para 79), with the only limitation of "compliance with EU law, in particular the rules on the free movement of goods set out in Articles 34 to 36 TFEU" (para 79). This conclusion apparently stems from art 5(3) of the Treaty of the European Union (TEU) and art 2 (2) TFEU; i.e., from the principle of subsidiarity and the rules applying to shared competences [see also Purnhagen et al. (2018b)]. Such interpretation has been already well described by the legal literature in relation to the EU legal regime on GMO [see, e.g., Sadeleer (2014) and Weimer (2019)] and was implicitly acknowledged by the Court in previous cases, like *Pioneer Hi Bred Italia*.[8] However, in *Pioneer Hi Bred Italia* the Court, even if bound by the same legal principles than in *Confédération paysanne and Others*, decides just in the opposite direction. The main reason motivating these diverging decisions seemingly derives from the fact that in *Pioneer Hi Bred Italia* the Court appreciates the "harmonized" (*Pioneer Hi Bred Italia*, para 5) nature of the matter at issue, while in *Confédération paysanne and Others* it does not (see *Confédération paysanne and Others*, para 79: "to the extent to which the EU legislature has not regulated those organisms […]"). Be that as it may, the interpretation of the Court in *Confédération paysanne and Others* was not the only possible reading of Directive 2001/18/EC in relation to mutagenesis.

Arts 5(3) TEU and 2(2) TFEU

- Art 5(3) TEU: "Under the principle of subsidiarity, in areas which do not fall within its exclusive competence, the Union shall act only if and in so far as the objectives of the proposed action cannot be sufficiently achieved by the Member States, either at central level or at regional and local level, but can rather, by reason of the scale or effects of the proposed action, be better achieved at Union level."
- Art 2(2) TFEU: "When the Treaties confer on the Union a competence shared with the Member States in a specific area, the Union and the Member States may legislate and adopt legally binding acts in that area. The Member States shall exercise their competence to the extent that the Union has not exercised its competence. The Member States shall again exercise their competence to the extent that the Union has decided to cease exercising its competence."

The Advocate General in its Opinion (see paras 115–117) frames two scenarios that in his view might explain the legislative positioning of the EU legislature in relation to mutagenesis: (a) "the EU legislature made a legislative choice. It carried out an evaluation, and on the basis of that evaluation came to the conclusion that all the mutagenesis techniques are to be excluded because they are safe" (Opinion, para 116); or, (b) "by inserting the mutagenesis exemption, the EU legislature did not make any statement about its safety" (para 117). The Advocate General compares the role of the EU legislature in the first scenario with that of "an architect that decided to have a room called 'mutagenesis' in his house, but who also decided to keep that room empty" (para 116); while in the second scenario, according

[8] Judgment of 6 September 2012, *Pioneer Hi Bred Italia*, C–36/11, EU:C:2012:534.

to the Advocate General, "the architect effectively decided to leave that space called 'mutagenesis' outside his house" (para 117). The first scenario amounts to full harmonization (see para 116 of the Opinion), while the second scenario would represent a lack of harmonization (see para 117 of the Opinion). Such scheme stems from the legal reasoning formerly mentioned (deriving from arts 5 (3) TEU and 2(2) TFEU) on the basis of the equilibrium on which the EU regime on GMO is built [i.e., the compromise between "[t] he protection of human health and the environment" (recital 5 Directive 2001/18/EC) and the principles governing the internal market in the EU (Salvi, 2016)]. However, the Court does not follow any of the options framed by the Advocate General. Instead, the Court decides to square the circle. Indeed, like the Advocate General, the Court is of the opinion that "the EU legislature has not regulated those organisms" (Judgment, para 79), but it assumes a safety assessment of the EU legislature as regards mutagenesis, manifested in recital 17 (see Judgment, paras 44, 45, 51, 54 and conclusion). In other words, the Court interprets art 3(1), Annex I B (1) and recital 17 Directive 2001/18/EC as a minimum threshold of harmonization (Purnhagen et al., 2018b), and therefore, according to the logic set in art 2(2) TFEU: "Member States shall again exercise their competence to the extent that the Union has decided to cease exercising its competence." Recouping the example of the Advocate General in its Opinion, "the EU legislator would be like an architect that decided to have a room called 'mutagenesis' in his house" (Opinion, para 116), but that instead of taking the decision "to keep that room empty" [as framed by the Advocate General (Opinion, para 116)], simply left it this way, and therefore, implicitly allowed EU Member States to furnish it (see Judgment, paras 44, 45, 51, 54, 79 and conclusion).

It could be argued that what the Court really has done is to transform an implicit preemption of action of Member States allegedly stemming from recital 17 Directive 2001/18/EC [equivalent to the above mentioned first scenario framed by the Advocate General (Opinion, para 116)], in a renounce of the EU legislature to regulate GMO obtained by means of traditional techniques of random mutagenesis. This interpretation is supported by the very late appearance of a case like *Confédération paysanne and Others*. In other words, if the possibility of traditional mutagenesis being regulated at a national level needed the pronunciation of the Court after so many years, then maybe the scenario of the EU legislature fully harmonizing those techniques should have been seriously considered by the Court as the most plausible option. However, this line of reasoning is somehow countered by the disharmonizing effect of Directive (EU) 2015/412 on the EU legal regime on GMO [see the Opinion of the Advocate General, para 122, Salvi (2016), Purnhagen et al. (2018b) and Wanner et al. (2019)], and, most importantly, this was not the interpretative path taken by the Court.

From the Judgment onwards, three categories of organisms matter in practice: *(1)* non-GMO; *(2)* GMO mentioned in art 3(1) Directive 2001/18/EC obtained through traditional techniques of random mutagenesis; *(3)* GMO falling within art 2(2) Directive 2001/18/EC [among which, according to the Court, organisms obtained by means of NBT are included (Urnov et al., 2018)]. Before the Judgment, varieties obtained by means of traditional techniques of random mutagenesis were claimed to be "an independent third category due to aspects of risk evaluation" (Spranger, 2015: 25), but that view is not clearly recognized in Directive 2001/18/EC, and there was no legal certainty on this issue until the Judgment. As observed by some scholars and breeders' associations [see, eg, Martin in Science Media Centre (2018); Gelinsky and Hilbeck (2018); CIOPORA (2018); Wanner et al. (2019), or Jorasch (2019)], from now on, according to the Judgement, GMO obtained by means of traditional mutagenesis will be able to be subjected by EU Member States "to the obligations laid down in that directive or to other obligations" (para 82 and conclusion 3). The Court is silent on GMO obtained through cell fusion (point (2) of Annex I B Directive 2001/18/EC), but it is foreseeable the interpretation of the Court extends to them.

This "reclassification" done by the Court might have in turn important implications. Indeed, because of the reference of the Court "to the obligations laid down in that directive [Directive 2001/18/EC] or to other obligations" (para 82 and conclusion 3), Member States might regulate the risk assessment of such varieties or its labelling at a national level, or subject them to other conditions and limitations. Furthermore, it cannot be ruled out that, as a result of the Judgment in connection to Directive (EU) 2015/412, the cultivation of such varieties end restricted or even prohibited at a national level in the same way as GM varieties within the scope of Directive 2001/18/EC [on the analysis of Directive (EU) 2015/412 see, e.g., Salvi (2016)]. In fact, in the light of the Judgment, mutant varieties bred through random mutagenesis might end being subjected "to other [national] national obligations" (para 82 and conclusion 3) potentially stricter and more burdensome than those stemming from Directive 2001/18/EC. It is clear from the aforesaid that the decision of the Court, in addition to further disharmonizing GMO regulation in the EU (Wanner et al., 2019), might also result, despite the condition introduced by the Court [of "compliance with EU law, in particular with the rules on the free movement of goods" (para 82)], in obstacles to the free movement of goods. If Member States end eventually following the possibility set by the CJEU as regards traditional mutant varieties, the free movement of goods [see Wanner et al. (2019)], plant innovation and agriculture [see Martin in Science Media Centre (2018)], and consumer choice in the EU, might be severely affected. Therefore, in that case, action should be taken at an EU level to reharmonize this area of the EU legal regime on GMO in order to impede or minimize the aforementioned potential negative impacts.

"Euphoria" in the Organic Sector

In a position paper issued before the Judgment, IFOAM stated that techniques falling within the category of "mutagenesis" are not "[a] cceptable for organic breeding" and "[t]o be phased out" (IFOAM Organics International, 2017: 20); and, shortly after the press release of the Judgment [see CJEU (2018)], showed its satisfaction with the position adopted by the Court [see IFOAM EU Group (2018b)]. However, after the Judgment, references to traditional mutagenesis (and to mutagenesis *lato sensu*) practically disappeared from IFOAM's communications [see, e.g., IFOAM EU Group (2018b) and IFOAM EU Group (2019)] despite IFOAM being apparently

well aware of the potential reach of the Judgment [see, e.g., IFOAM EU Group (2018a)]. In the light of it, it cannot be excluded that the Court might have gone even further than some players of the organic sector wished. It must not be forgotten that at a worldwide level there are at least 3318 registered varieties obtained through traditional mutagenesis, 55% of them breed before 1990 (IAEA).

The Concept of GMO After the Judgment: The Mutagenesis Exemption

In **Table 1**, the concept of GMO under Directive 2001/18/EC as interpreted by the Court is schematized through the criteria that may end with an exemption from the scope of Directive 2001/18/EC. Construed from the legal analysis of the Judgment carried out in this paper, **Table 1** systematizes the interpretative efforts reflected in the literature [New Techniques Working Group (2012); Krämer (2015); Spranger (2015); Krämer (2015); Spranger (2015); Vives-Vallés (2016); Vives-Vallés (2018), Purnhagen et al. (2018a; 2018b), Sprink et al. (2016); Eriksson et al. (2018); Eriksson (2018); Wanner et al. (2019); Custers et al. (2019), etc.] and adapts them either to the situation post Judgment and/or to the purpose of the table. It is worth noting that the reasoning portrayed in **Table 1** is not new, but it was already anticipated by Krämer (2015) and Spranger (2015) to a great extent. Krämer (2015) and Spranger (2015) detected already in 2015 that the key to understand the concept of GMO of Directive 2001/18/EC are not as much the descriptions contained in arts 2(2) and 3, but mainly the logical scheme set in those articles plus their annexes (i.e., whether the lists they refer to/contain are open or closed) interpreted in the light of the precautionary principle and recital 17 Directive 2001/18/EC. Some of these aspects have been also pointed out, before and after the Judgment, by other scholars [see, eg, New Techniques Working Group (2012); Vives-Vallés (2016) or Purnhagen et al. (2018a; 2018b)]. Therefore, according to the Court, how natural those techniques may be is not determinant (Custers et al., 2019) and the techniques listed in Annex I A Part 1 do not exhaust the notion of (nonexempted) GMO of art 2(2)(a) Directive 2001/18/EC. It is instead the inability of those techniques to fit in Annex I A Part 2 and Annex I B Directive 2001/18/EC, that matters the most (see **Table 1**). Certainly, the Court considered in its assessment the definition in art 2(2) Directive 2001/18/EC, mentioning in fact the three requirements it contains [i.e., "alterations made to the genetic material of an organism" (para 28 of the Judgment), "with the exception of human beings" (para 27), and "in a way that does not occur naturally" (para 29)];

TABLE 1 | Cumulative criteria that genetic engineering/breeding techniques must meet in order to be excluded from the scope of Directive 2001/18/EC as interpreted by the CJEU in the Judgment.

Order/ Question	Criteria	Result
1)	Does it result in "an organism […] in which the genetic material has been altered"?	Negative answer: Out of the scope of Directive 2001/18/EC. Affirmative answer: Check requirement "2)."
2)	Does it refer to an implementation on "human beings"? ("exception" contained in art 2(2) 2001/18/EC)	Affirmative answer: Out of the scope of Directive 2001/18/EC. Negative answer: Check requirement "3)."
3)	Does it fit in any of the techniques listed in Annex I A Part 1 Directive 2001/18/EC?	Affirmative answer: Within the scope of Directive 2001/18/EC (i.e., art 2(2)(a) Directive 2001/18/EC). Negative answer: Check requirement "4)."
4)	Does it fit in any of the techniques listed in Annex I A Part 2 Directive 2001/18/EC?	Affirmative answer: Out of the scope of Directive 2001/18/EC. Negative answer: Check requirement "5)."
5)	Does it fit in the notion of "mutagenesis" or "cell fusion (including protoplast fusion) of plant cells of organisms which can exchange genetic material through traditional breeding methods"?	Negative answer: Within the scope of Directive 2001/18/EC (i.e., art 2(2)(a) Directive 2001/18/EC). Affirmative answer: Check requirement "6)."
6)	Does it "involve the use of recombinant nucleic acid molecules or genetically modified organisms other than those produced by one or more of the techniques/methods listed" in Annex I B Directive 2001/18/EC?	Affirmative answer: Within the scope of Directive 2001/18/EC (i.e., art 2(2)(a) Directive 2001/18/EC). Negative answer: Check requirement "7)."
7)	Has it "conventionally been used in a number of applications"?	Negative answer: Within the scope of Directive 2001/18/EC (i.e., art 2(2)(a) Directive 2001/18/EC). Affirmative answer: Check requirement "8)."
8)	Has it "a long safety record"?	Negative answer: Within the scope of Directive 2001/18/EC (i.e., art 2(2)(a) Directive 2001/18/EC). Affirmative answer: Exempted from the scope of Directive 2001/18/EC (on the basis of art 3(1) Directive 2001/18/EC). It may still be subjected "to the obligations laid down in that directive [Directive 2001/18/EC] or to other obligations" by EU Member States (Judgment, para 82 and conclusion 3).

"Order/Question": Logical order in which the criteria must be assessed for a given technique. "Criteria", Criteria, framed as a question to be answered, that a given technique must meet in order to be excluded from the scope of Directive 2001/18/EC. "Result": Legal consequence or action to be taken depending of the fulfilment or not of the relevant criterion (i.e., depending on the answer to the relevant question under the column "Criteria").

but the two first requirements (in paras 27 and 28) are basically prerequirements, and the importance of the third requirement (in para 29) is somehow watered down by the reference of the Court to "the general scheme of that directive [Directive 2001/18/EC]" (para 31) developed in paras 31 to 37 of the Judgment. The consequence of this interpretation is that, as anticipated by Krämer (2015) and Spranger (2015), a technique will lead to a nonexempted GMO (falling within art 2(2)(a) in connection to Annex I A Part 1 Directive 2001/18/EC) if such technique cannot be classified in Annex I A Part 2 nor in Annex I B Directive 2001/18/EC (see **Table 1**). In other words, a dynamic interpretation of the annexes as regards the techniques covered by them is mandatory for Annex I A Part 1 and not possible for the other annexes (Spranger, 2015). It is worth mentioning that, as implicitly acknowledged by the Court (see Judgment, paras 27–38, 40), what is to be understood by "mutagenesis" has nothing to do with the use of "recombinant nucleic acids" (NA) or "genetically modified organisms" (Annex I B Directive 2001/18/EC). Besides, for a GMO produced by means of mutagenesis to be excluded from the scope of Directive 2001/18/EC, in addition to the fulfilment of recital 17, the "condition that they do not involve the use of recombinant nucleic acid molecules or GMOs other than those produced by one or more of the techniques/methods listed in that annex [Annex I B]" (Judgment, para 40) must also be met (see **Table 1**). This was also foreseen by Krämer (2015) and Spranger (2015) and observed after the Judgment by Eriksson (2018). The Judgment however, even if mentioning all these requirements from Annex I B and recital 17, does not elaborate on any of them. Regarding "the condition that they do not involve the use of recombinant nucleic acid molecules" (Annex I B Directive 2001/18/EC), Krämer (2015) explains that Council Directive 90/220/EEC does not contain it and that its inclusion in Directive 2001/18/EC must be understood as "a supplementary requirement […] to enlarge the field of application of Directive 2001/18 and to reduce the exemption of Article 3 and Annex I B" (Krämer, 2015: 12). As regards recital 17, Directive 2001/18/EC does not provide any guidance on its interpretation (Krämer, 2015); but it makes sense to interpret it as containing two different, but cumulative (i.e., both of them must be fulfilled), requirements (Krämer, 2015). Fulfilling "a number of applications" only is not enough [see Krämer (2015)]. Additionally, those applications must "have a long safety record" [see Krämer (2015)]. Directive 2001/18/EC does not explain either how recital 17 must be assessed Krämer (2015). A reading of recital 17 Directive 2001/18/EC coherent with the Judgment [as well as with the position taken by Krämer (2015) and Spranger (2015)] suggests that, somehow, the first requirement in recital 17 (i.e., "a number of applications") should refer to the diversity of the applications, while the second requirement in recital 17 (i.e., "a long safety record") might be connected to the number of records within each application as well as to the proven degree of "safety" of each application. It also must be noted that Annex I B refers to "the use of recombinant nucleic acid molecules or genetically modified organisms" but not to "[t]echniques of genetic modification" like Annex I A Part 1; therefore, those techniques of genetic modification that "do not involve the use of recombinant nucleic acid molecules or genetically modified organisms" (as mandated in Annex I B) and fitting also within the scientific notion of "mutagenesis," should be deemed potentially coverable by Annex I B [see also Purnhagen et al. (2018b)], subjected only to the fulfilment of the requirements in recital 17. Besides, according to the Judgment (see also **Table 1**), the techniques listed in Annex I B must be deemed always included in art 2(2)(a) Directive 2001/18/EC (see Judgment, paras 27–38), and only excluded from the scope of Directive 2001/18/EC as long as they meet the requirements stemming from recital 17 (paras 43–48) and mentioned in Annex I B Directive 2001/18/EC (para 40). The Judgment though, does not provide any guidance on what is to be understood by to "not involve the use of recombinant nucleic acid molecules or genetically modified organisms other than those produced by one or more of the techniques/methods listed" in Annex I B Directive 2001/18/EC; nor on how should the requirements in recital 17 Directive 2001/18/EC be assessed. The term "mutagenesis" is not addressed in the Judgment either.

Dynamic interpretation of law

The dynamic interpretation of law is an interpretative approach which maintains that "the real meaning of a legal norm can be best disclosed at the moment of its interpretation" (Harašić, 2015: 35). It therefore pays attention to the "present societal, political, and legal context" of the legal texts under interpretation (Eskridge, 1987: 1479).

Annex I A Part 1 Directive 2001/18/EC

"TECHNIQUES REFERRED TO IN ARTICLE 2(2)

PART 1

Techniques of genetic modification referred to in Article 2(2)(a) are inter alia:

1. recombinant nucleic acid techniques involving the formation of new combinations of genetic material by the insertion of nucleic acid molecules produced by whatever means outside an organism, into any virus, bacterial plasmid or other vector system and their incorporation into a host organism in which they do not naturally occur but in which they are capable of continued propagation;
2. techniques involving the direct introduction into an organism of heritable material prepared outside the organism including microinjection, macroinjection, and microencapsulation;
3. cell fusion (including protoplast fusion) or hybridization techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not occur naturally."

Annex I A Part 2 Directive 2001/18/EC

"TECHNIQUES REFERRED TO IN ARTICLE 2(2)

[…]

PART 2

Techniques referred to in Article 2(2)(b) which are not considered to result in genetic modification, on condition that they do not involve the use of recombinant nucleic acid molecules or genetically modified organisms made by techniques/methods other than those excluded by Annex I B:

1. *in vitro* fertilization,
2. natural processes such as: conjugation, transduction, transformation,
3. polyploidy induction."

Leeway to Operate Out of the Scope of Directive 2001/18/EC Post Judgment

Several additional teachings deduced from the Judgment might be relevant to further clarify the situation of GMO and plant breeding in the EU, and to assess the possibility to operate out of the scope of Directive 2001/18/EC.

First, although it is indisputable that a dynamic interpretation of Annex I B Directive 2001/18/EC to include additional techniques not listed in it is not possible [see Spranger (2015) and Judgment, paras 40ff], this obstacle does not necessarily apply to the interpretation of the techniques already present in such annex nor to the requirements included or applying to the annex. Certainly, the Court does not expressly take a position on this issue (Wanner et al., 2019), but it does not close the door to a dynamic interpretation of these later aspects either. Several issues must be differentiated, particularly: flexibility as regards the definition of the techniques cited in Annex I B (i.e., what is to be understood by "mutagenesis" and "cell fusion […]"); flexibility applying to the requirements from recital 17 (i.e., what is to be understood by "a number of applications" and by "a long safety record"); and flexibility in relation to the requirements stemming from the very annex (i.e., (1) "do not involve the use," (2) "recombinant nucleic acid molecules," and (3) "genetically modified organisms other than those produced by one or more of the techniques/methods listed" in Annex I B Directive 2001/18/EC).

With respect to the concept of "mutagenesis," it must be noted that the Court recognizes the vagueness of Directive 2001/18/EC (see Judgment, para 43: "by referring generally to mutagenesis, that provision does not, on its own, provide any conclusive guidance as to the types of techniques/methods […]"). Indeed, Directive 2001/18/EC does not address the concept of "mutagenesis" (Krämer, 2015; Spranger, 2015; Purnhagen et al. 2018b; Eriksson, 2018; Eriksson et al., 2018); but the Court implicitly admits that, at least some applications of these NBT, might eventually fit within the notion of "mutagenesis" from Directive 2001/18/EC (see the references to "new techniques/methods of mutagenesis" (Judgment, paras 48, 51, and 53) as well as the reasoning of the Court in paras 28–38).

As for the requirements stemming from recital 17 Directive 2001/18/EC in relation to the exemption of "mutagenesis" by art 3(1) in relation to Annex I B Directive 2001/18/EC, it must be remarked that if the Court had chosen to interpret them in a static way, it would rather have circumscribed its assessment to the time period prior to the approval of the Directive, but it decided instead to take into account later circumstances [see Judgment, paras 47 ("[…] thus far […]"), 48 ("[…] might prove […]"), 51 ("In those circumstances, […]"), and 53 ("[…] might be […]")]. Furthermore, as remarked by Purnhagen et al. (2018a), the Court concludes by stating "that only organisms obtained by means of techniques/methods of mutagenesis which have conventionally been used in a number of applications and have a long safety record are excluded from the scope of that directive" (first conclusion, second para). Such statement is also coherent with a choice of a dynamic approach to the interpretation of Directive 2001/18/EC. If the Court had followed a static interpretation of the law, it would most likely have expressly excluded techniques used before a certain date (e.g., 2001 or 1990) or specific techniques or groups of techniques (e.g., irradiation or chemical-induced mutagenesis techniques). Furthermore, the wording used by the Court is not the result of constraints stemming from the questions referred by the *Conseil d'État* either (cf. Judgment, para 25 and conclusions). It must be deduced from the foregoing that the Judgment does not prevent the possibility of a dynamic interpretation of the techniques within Annex I B as regards the requirements stemming from recital 17.

Static interpretation of law

Static legal interpretation may be defined as an interpretative approach based on the idea of the "sense […] that the norm had at the time of its adoption" as its true "sense" or meaning (Harašić, 2015: 35).

Regarding the requirements contained in Annex I B Directive 2001/18/EC, the Court only mentions them by quoting the content of the annex (Judgment, para 40), and therefore no specific guidance is provided, but flexibility is neither preempted.

Second, it is clear from the aforesaid as well as from other passages of the Judgment (see, e.g., paras 53, 54 and conclusion 3), that the critical motive founding the refusal of the Court to exclude NBT from the scope of Directive 2001/18/EC is the alleged lack of "certainty" (Judgment, para 47) regarding the requirements comprised in recital 17 Directive 2001/18/EC (see paras 45, 51, 53 and conclusion 3). Therefore, if at some point those requirements imposed by recital 17 on "new techniques/methods" fitting within Annex I B Directive 2001/18/EC are proven with a reasonable degree of "certainty", according to the teachings of the Judgment, those techniques might be excluded from the scope of Directive 2001/18/EC. However, in the light of the Judgment (see paras 50ff), even in the case of an NBT or a group of NBT eventually meeting all criteria [from recital 17 and the other applicable criteria from Directive 2001/18/EC (see **Table 1** and preceding section)], some action by the EU legislature is needed for that exclusion be feasible. We propose that a new EU directive or regulation is passed, ascertaining the fulfilment of the criteria contained in Annex I B Directive 2001/18/EC and in recital 17 Directive 2001/18/EC (listed in **Table 1**) by the relevant technique/s. This line of action is also considered by experts to be the only, or at least, the most feasible way of finding some leeway to operate with NBT out of the scope of Directive 2001/18/EC post Judgment (Purnhagen, personal com.). Such approach might be implemented within the framework of Directive 2001/18/EC as interpreted by the Judgment, without the need of a change of paradigm nor even the amendment of the scheme of Directive 2001/18/EC. Therefore, considering that a reform of Directive 2001/18/EC would be probably a lengthy process (Eriksson et al., 2018), and that such delay would have a negative impact on plant breeding (Eriksson et al., 2018), this proposal could likely work as a

suitable transitory solution until a deeper reform of the EU legal regime on GMO comes. In the absence of further guidance by the CJEU on the concept of "mutagenesis" as well as of the requirements contained in Annex I B Directive 2001/18/EC, choices among the different possible interpretations (Krämer, 2015; Spranger, 2015; Jorasch, 2016; Sprink et al., 2016; Eriksson, 2018; Eriksson et al., 2018; Custers et al., 2019) will have to be made by the EU legislature. Defining in detail these choices falls completely out of the scope of the present paper; but, in the following section, the status of the most well-known breeding techniques (see **Table 2**) in the light of the aforementioned criteria from Directive 2001/18/EC interpreted according to the Judgment (see **Table 1**) is shown, further illustrating the potential reach of a limited legislative proposal like the one outlined.

Analysis of the Impact of the Judgment on the Breeding Techniques

Provided that off-targeting effects and associated risks are appropriately managed, ODM, SDN1, and SDN2 are the only groups of techniques from **Table 2** with the potential to render certain applications exemptible from the scope of Directive 2001/18/EC by means of a limited legislative proposal not altering the EU GMO scheme. This conclusion has been reached through the analysis of a nonexhaustive list of plant breeding techniques mentioned in Directive 2001/18/EC, in SAM (2017) and in other sources (see **Table 2**), on the basis of the following criteria defining their status under Directive 2001/18/EC in the light of the Judgment:

- "History of use in plant breeding": approximate time when the technique has started to be used for plant breeding (indicative publication of the first application in plants, on the basis of a search of the relevant literature on the topic). It is not meant to substitute (nor it can substitute) the assessment to be done by the EU legislature on the fulfilment of the requirements contained in recital 17 Directive 2001/18/EC. Only proposed as a proxy of the requirements stemming from recital 17 Directive 2001/18/EC for indicative purposes in the strict framework of the theoretical exercise carried out in this section. Related to questions "7)" and "8)" from **Table 1**.
- "Annex I A Part 1 Directive 2001/18/EC?": "Does it fit in any of the techniques listed in Annex I A Part 1 Directive 2001/18/EC?" (see **Table 1**): No, yes (expressly mentioned) [expressly mentioned in Annex I A Part 1 Directive 2001/18/EC], yes (recital 17 not ascertained) [recital 17 Directive 2001/18/EC not ascertained by the EU legislature or the Judgment], yes (not in the other annexes) [it does not fit in the other annexes from Directive 2001/18/EC (see reasoning in **Table 1** and related section)], or, yes (but exempted) [it is a GMO technique according to Directive 2001/18/EC as interpreted by the Judgment, but Directive 2001/18/EC expressly exempts the technique by means of Annex I B)]. Related to question "3)" from **Table 1**.
- "Annex I A Part 2 Directive 2001/18/EC?": "Does it fit in any of the techniques listed in Annex I A Part 2 Directive 2001/18/EC" (see **Table 1**): Yes or no. Related to question "4)" from **Table 1**.
- "'[M]utagenesis' or 'cell fusion […]'?": "Does it fit in the notion of "mutagenesis" or "cell fusion (including protoplast fusion) of plant cells of organisms which can exchange genetic material through traditional breeding methods"?" (see **Table 1**): No, yes ("mutagenesis"), or yes ("cell fusion […]"). Related to question "5)" from **Table 1**.
- "'[I]nvolve […] recombinant nucleic acid molecules' (recNA)": DNA or RNA sequences containing genetic elements whose sequence and/or combination were not originally present in the species genome. (Some authors propose other definitions restricting the evaluation to the genome of the individual (not the species) or allowing to consider as nonrecombinant sequences declared as "near-identical" (Eriksson, 2018: 387) based on a threshold estimated according to the size of the genome [Eriksson, 2018)]: Yes, no, or no* ("no*" means that under a broader interpretation of "recombinant nucleic acid molecules" (e.g., when the evaluation is restricted to the genome of the individual itself), it could be a "yes"). Related to question "6)" from **Table 1**.
- "'[U]se' *lato sensu* of recNA": "use of recombinant nucleic acid molecules" (*lato sensu*), i.e., introduction in the plant of DNA or RNA sequences (but not insertion of heritable recombinant DNA sequences into the genome). Related to question "6)" from **Table 1**.
- "'[U]se' *stricto sensu* of recNA": "use of recombinant nucleic acid molecules" (*stricto sensu*), i.e., stable insertion of heritable DNA sequences into the genome. Related to question "6)" from **Table 1**.
- "Classification according to Directive 2001/18/EC": classification of the techniques in Directive 2001/18/EC interpreted according to the Judgment (see **Table 1** and preceding sections).
- "Out of the scope of Directive 2001/18/EC?": status of the techniques as regards the scope of Directive 2001/18/EC interpreted according to the Judgment: yes (non-GMO), yes (exempted GMO) [exempted GMO, although according to the Judgment (conclusion 3) they may still be subjected "to the obligations laid down in that directive [Directive 2001/18/EC] or to other obligations"], or no (nonexempted GMO).
- "Potentially exemptible?": Possibility to exclude a technique if the requirements stemming from recital 17 Directive 2001/18/EC are ascertained by the EU legislature according to the legislative proposal outlined in the present paper (based on the analysis of the Judgment, Directive 2001/18/EC and the literature (see previous sections as well as **Table 1**): No, Yes, Yes* (provided that a too broad interpretation of the requirements contained in Annex I B Directive 2001/18/EC is not adopted), or – (it does not apply because already exempted or non-GMO according to Directive 2001/18/EC interpreted according to the Judgment).

TABLE 2 | Plant breeding techniques comparison according to criteria defining their status under Directive 2001/18/EC in the light of the Judgment.

Breeding Technique	History of use in plant breeding	Annex I A Part 1 Directive 2001/18/EC?	Annex I A Part 2 Directive 2001/18/EC?	"[M]utagenesis" or "cell fusion […]"?	"[I]nvolve […] recombinant nucleic acid molecules"	"[U]se" *lato sensu* of recNA (introduction in the plant of DNA or RNA sequences)?	"[U]se" *stricto sensu of* recNA (stable insertion of "heritable" DNA sequences)?	Classification according to Directive 2001/18/EC	Out of the scope of Directive 2001/18/EC?	Potentially exemptible?
Crossing and selection (classical breeding)	Since 1870's (Mendel, 1901)	No	Yes	No	No	No	No	Art 2(2) + Annex I A Part 2	Yes	–
In vitro fertilization	Since 1930's (Sharma et al., 1996)	No	Yes	No	No	No	No	Art 2(2)(b) + Annex I A Part 2	Yes	–
Polyploidy induction	Since 1940's (Blakeslee and Avery, 1937)	No	Yes	No	No	No	No	Art 2(2)(b) + Annex I A Part 2	Yes	–
Random mutagenesis (chemicals, radiations)	Since 1930's (Stadler, 1928)	yes (but exempted)	No	Yes ("mutagenesis")	No	No	No	Art 3(1) + Annex I B	Yes (exempted GMO)	–
Protoplasts fusion between sexually compatible species	Since 1970's (Carlson et al., 1972)	yes (but exempted)	No	Yes ("cell fusion […]")	No	No	No	Art 3(1) + Annex I B	Yes (exempted GMO)	–
Protoplasts fusion between sexually incompatible species	Since 1970's (Carlson et al., 1972)	yes (because not in the other annexes)	No	No	No	No	No	Art 2(2)(a) + Annex I A Part 1	No	No
"Classical" transgenesis	Since 1980's (Zambryski et al., 1983)	yes (expressly mentioned)	No	No	Yes	Yes	Yes	Art 2(2)(a) + Annex I A Part 1	No	No
Microinjection/macroinjection and microencapsulation	Since 1980's (Reich et al., 1986)	yes (expressly mentioned)	No	No	Yes[a]	Yes	Yes/No[b]	Art 2(2)(a) + Annex I A Part 1	No	No
Agro-infiltration	Since 1990's (Grimsley et al., 1986)	yes (not in the other annexes)	No	No	Yes	Yes	No	Art 2(2)(a) + Annex I A Part 1	No	No
Oligonucleotide-Directed Mutagenesis (ODM)	Since 2000's (Zhu et al., 1999)	yes (recital 17 not ascertained)	No	Yes ("mutagenesis")	Yes/No*[c]	Yes/No[c]	No	Art 2(2)(a) + Annex I A Part 1	No	Yes*
Intragenesis	Since 2000's (Rommens et al., 2007)	yes (not in the other annexes)	No	No	Yes	Yes	Yes	Art 2(2)(a) + Annex I A Part 1	No	No
Cisgenesis	Since 2000's (Schouten et al., 2006)	yes (not in the other annexes)	No	No	No* (if no T-DNA)	No (if no T-DNA)	No (If no T-DNA)	Art 2(2)(a) + Annex I A Part 1	No	No
Transgrafting (GM scion on non-GM rootstock, or vice-versa)	Since 2000's (Lifschitz et al., 2006)	yes (not in the other annexes)	No	No	Yes	Yes/No (depends on the part harvested)	Yes/No (depends on the part harvested)	Art 2(2)(a) + Annex I A Part 1	No	No
Reverse breeding	Since 2010's (Dirks et al., 2009)	yes (not in the other annexes)	No	No	Yes	No (in the final product)	No (in the final product)	Art 2(2)(a) + Annex I A Part 1	No	No

(Continued)

TABLE 2 | Continued

Breeding Technique	History of use in plant breeding	Annex I A Part 1 Directive 2001/18/EC?	Annex I A Part 2 Directive 2001/18/EC?	"[M]utagenesis" or "cell fusion […]"?	"[I]nvolve […] recombinant nucleic acid molecules"	"[U]se" *lato sensu* of recNA (introduction in the plant of DNA or RNA sequences)?	"[U]se" *stricto sensu of* recNA (stable insertion of "heritable" DNA sequences)?	Classification according to Directive 2001/18/EC	Out of the scope of Directive 2001/18/EC?	Potentially exemptible?
Gene editing: Targeted mutagenesis using site-directed nucleases (SDN1) without insertion of the nuclease gene (transient transformation, RNA, RNP (ribo-nucleo protein), null segregant)	Since 2010's (Jiang et al., 2013; Woo et al., 2015)	yes (recital 17 not ascertained)	No	Yes ("mutagenesis")	Yes/No*[c]	Yes/No[c]	Yes/No[c]	Art 2(2)(a) + Annex I A Part 1	No	Yes*
Gene editing: Targeted mutagenesis using site-directed nucleases (SDN1) with insertion of the nuclease gene	Since 2010's (Shan et al., 2013)	yes (not in the other annexes)	No	No	Yes	Yes	Yes	Art 2(2)(a) + Annex I A Part 1	No	No
Gene editing: Allele swap using site-directed nucleases (SDN2) without insertion of the nuclease gene (transient transformation, RNA, RNP (ribo-nucleo protein), null segregant)	Since 2010's (Shi et al., 2017)	yes (recital 17 not ascertained)	No	Yes ("mutagenesis")	Yes/No*[c]	Yes/No[c]	Yes/No[c]	Art 2(2)(a) + Annex I A Part 1	No	Yes*
Gene editing: Allele swap using site-directed nucleases (SDN2) with insertion of the nuclease gene	Since 2010's (Shi et al., 2017)	yes (not in the other annexes)	No	No	Yes	Yes	Yes	Art 2(2)(a) + Annex I A Part 1	No	No
Gene editing: Targeted transgenesis using site-directed nucleases (SDN3)	Since 2010's (Li et al., 2013)	yes (not in the other annexes)	No	No	Yes	Yes	Yes	Art 2(2)(a) + Annex I A Part 1	No	No
Gene regulation using site-directed effectors (activators/repressors /epigenetic factors)	Since 2010's (Piatek et al., 2015)	yes (not in the other annexes)	No	No	Yes	Yes	Yes/No[d]	Art 2(2)(a) + Annex I A Part 1	No	No
Gene regulation using site-directed nucleases targeting RNAs (SDN4) (stable integration)	Being developed (Shmakov et al., 2015)	yes (not in the other annexes)	No	No	Yes	Yes	Yes	Art 2(2)(a) + Annex I A Part 1	No	No
RNA dependent DNA methylation (RdDM)	Being developed (Ruiz-Ferrer and Voinnet, 2009)	yes (not in the other annexes)	No	No	Yes	Yes	Yes/No[d]	Art 2(2)(a) + Annex I A Part 1	No	No
Genome editing using site-directed recombinases	Being developed in animals, soon plants (Mercer et al., 2012)	yes (not in the other annexes)	No	No	Yes	Yes	No[d]	Art 2(2)(a) + Annex I A Part 1	No	No

[a]*Initially, these techniques were developed to transfer "recombinant nucleic acid molecules".*

[b]*Provided that a stable insertion is not carried out.*

[c]*"No" provided that the allele sequence is already present in the species gene pool.*

[d]*"No" in case of transitory transformation or null segregant.*

Nonexhaustive list of plant breeding techniques mentioned in Directive 2001/18/EC, in SAM (2017) and new approaches currently being developed, the descriptions of which can be found in the references mentioned inside the table. All the techniques listed result in "an organism […] in which the genetic material has been altered" (see question "1)" in ***Table 1****).*

It is worth noting that the exemption or deregulation of ODM, SDN1, and SDN2 techniques (see **Table 2**) was already proposed before the Judgment [see, e.g., Eriksson (2018) and Purnhagen et al. (2018b)]. The current proposal is based on the criteria extracted from Directive 2001/18/EC as interpreted by the Judgment (see **Table 1** and preceding sections), and therefore is adapted to the current understanding of the EU legal scheme on GMO. But, in order to that exemption may work in the context of a limited legislative proposal like the one outlined, the implementation of those techniques must be limited in a way that the requirements contained in Annex I B Directive 2001/18/EC are fulfilled. In other words, only those applications of ODM, SDN1, and SDN2 that may be assimilated to mutagenesis, and that "do not involve the use of recombinant nucleic acid molecules or GMOs […]" [see also Purnhagen et al. (2018b)] would be exemptible in the framework of such limited legislative proposal. It must be mentioned that, as the aforementioned techniques are based on recombinant DNA (Zhu et al., 1999; Shan et al., 2013; Shi et al., 2017), a broad interpretation of the condition "do not involve the use of recombinant nucleic acid molecules" (Annex I B Directive 2001/18/EC) would preempt the possibility of exempting any of the aforementioned techniques (see **Table 2**) without an amendment of the scheme of Directive 2001/18/EC. However, as the EU legislature did not precise what is to be understood by "not involve the use" and by "recombinant nucleic acid molecules" [see, e.g., Krämer (2015); Spranger (2015) and Eriksson (2018)], there is some margin of maneuver left to further define the condition to "not involve […] recombinant nucleic acid molecules," without being compelled to alter the scheme of Directive 2001/18/EC. But to achieve it, in addition to the requirements within Annex I B Directive 2001/18/EC, those requirements coming from recital 17 Directive 2001/18/EC (i.e., "conventionally […] used in a number of applications and […] a long safety record") should be also ascertained. The recent appearance of the techniques [especially SDN1 and SDN2 (see **Table 2**)] might be perceived as a complication. However, Directive 2001/18/EC does not define how the requirements within recital 17 should be interpreted (Spranger, 2015). This means that, as long as an optimum level of "safety" is ensured, fixing the desirable threshold of those

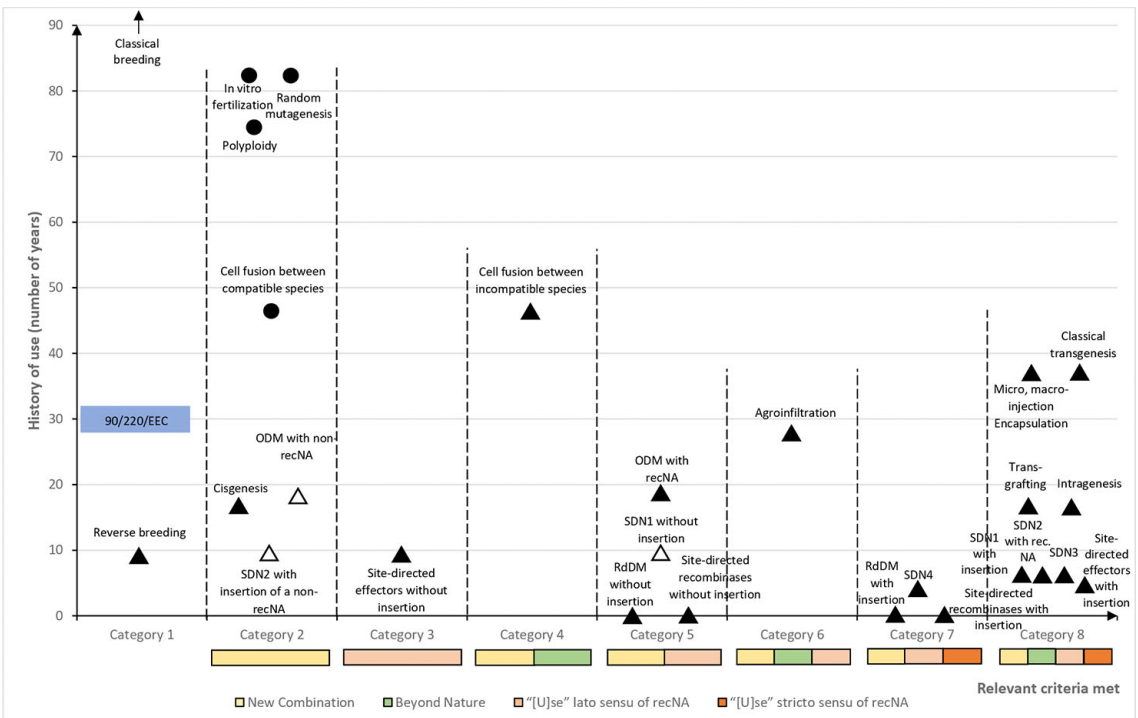

FIGURE 1 | Plant breeding techniques categorized according to their history of use and criteria potentially defining their legal status. For each category of breeding techniques, criteria potentially defining their status are marked as colored bars (the sizes of which do not refer to their level of risk). Categories are arbitrarily positioned on the x-axis according to the typology and cumulation of fulfilled criteria. Each plant breeding technique is placed on the graph according to the category it belongs to, and to its history of use: black triangles and circles represent respectively techniques that are currently under the scope of Directive 2001/18/EC and exempted according to the present study, while white triangles represent techniques which could be exempted by means of a limited legislative proposal (see **Table 1** and preceding sections). Legend of the x-axis: "New Combination": creation of a genetic variation (sequence, location) that was not present initially in the genome (see Custers et al. (2019); "Beyond nature": genetic "[a]teration beyond what does occur naturally by mating and/or natural recombination" (Custers et al., 2019); "[U]se" *lato sensu* of recNA: "use of recombinant nucleic acid molecules" (*lato sensu*), i.e., introduction in the plant of DNA or RNA sequences, but not insertion of heritable recombinant NA sequences into the genome (related to question "6)" from **Table 1**); "[U]se" *stricto sensu* of recNA: "use of recombinant nucleic acid molecules" (*stricto sensu*), i.e., stable insertion of heritable DNA sequences into the genome (related to question "6)" from **Table 1**).

requirements is strictly a matter of legislative policy. Furthermore, it must be noted that while random mutagenesis, polyploidy and *in vitro* fertilization were rather old techniques in the nineties when the EU legal regime on GMO was born, cell fusion was just coming of age at that time (see **Table 2** and **Figure 1**). In other words, if time since the discovery and/or the popularization of the (old) breeding techniques was not an issue when the Directive was approved, it should not be a problem now with the new techniques.

In summary, the analysis of the Judgment (in the section *Interpretation of the Judgment of the CJEU of 25 July 2018*) and the reasoning and justification of the limited legislative proposal (in the section *Leeway to Operate Out of the Scope of Directive 2001/18/EC Post Judgment*) shows that such proposal, launched as a transient solution until a reform arrives, is feasible from a legal perspective. The analysis carried out in the section *Analysis of the Impact of the Judgment on the Breeding Techniques* evinces that, although fairly limited, the proposal might be also meaningful for plant breeders, providing at least some leeway to the industry.

CONCLUSIONS

By considering targeted mutagenesis and varieties bred through these techniques as not exempted from the scope of Directive 2001/18/EC (Urnov et al., 2018), the Judgment will certainly have implications on these techniques; but, as observed by some scholars [see Martin in Science Media Centre (2018); Gelinsky and Hilbeck (2018) and Wanner et al. (2019)] as well as by CIOPORA (2018) and Jorasch (2019) from Euroseeds, it may also have an impact on traditional techniques of random mutagenesis and varieties thereof, as, from now on, varieties bred by means of traditional techniques of random mutagenesis, no matter how long they have been used, might be subjected "to the obligations laid down in that directive [Directive 2001/18/EC] or to other obligations" by EU Member States (Judgment, para 82 and conclusion 3). Although the interpretation of Directive 2001/18/EC provided by the Court is coherent with the principles governing the EU legal regime on GMO [see, e.g., Purnhagen et al. (2018a) and Eriksson (2018)], as shown by the Advocate General in its Opinion (see paras 115-117), it was not the only possible interpretation of Annex I B Directive 2001/18/EC. From now on, almost any aspect concerning those varieties (their risk assessment, labelling, cultivation, etc.) might be regulated at a national level. Even the application of Directive (EU) 2015/412 to those varieties, or stricter rules created at a national level, might eventually be dictated by Member States. Apparently though, since the Judgment came out, Member States have not regulated in that sense, and the organic sector does not seem to have urged them to proceed in that way either.

As regards NBT, the EU might consider to exempt certain techniques from the scope of Directive 2001/18/EC. In our opinion, it is clear that the Court does not dispute the classification of certain applications of NBT as a variant or species of "mutagenesis," i.e., targeted mutagenesis; and that the reason leading to consider them as not exempted is the nonfulfilment of the requirements stemming from recital 17 Directive 2001/18/EC. Therefore, if those techniques are "used in a number of applications and […] a long safety record" is ascertained, they could be exempted from the scope of Directive 2001/18/EC (provided that the specific applications of those breeding techniques fit within the concept of "mutagenesis" and comply with the requirements contained in Annex I B Directive 2001/18/EC). The analysis of the breeding techniques performed in this study shows that certain applications of ODM, SDN1, and SDN2 techniques potentially falling within the notion of mutagenesis and that "do not involve the use of recombinant nucleic acid molecules or GMOs […]" could be exempted without amending the scheme of Directive 2001/18/EC. Approving a supplementary EU regulation or directive ascertaining that those techniques comply with the conditions stemming from recital 17 Directive 2001/18/EC would suffice. Certainly, even if the proposal here outlined is eventually approved, the minimum demands of the breeding sector would not be appeased by its implementation. Furthermore, it must not be forgotten that a narrow interpretation of the conditions laid down in Annex I B Directive 2001/18/EC (particularly, "do not involve the use of recombinant nucleic acid molecules"), would make the proposal unfeasible. However, if it were successfully enforced, considering that years might pass until a reform of EU legal system on GMO succeeds (Eriksson et al., 2018), and that this delay would aggravate the situation of plant breeding in the EU (Eriksson et al., 2018), such limited legislative proposal might work at least as a quick interim solution, and provide some temporary leeway to operate outside the scope of Directive 2001/18/EC.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article/supplementary material.

AUTHOR CONTRIBUTIONS

JV-V designed the study, performed the analysis of the Judgment, participated in the analysis of the techniques, and wrote the paper. CC performed the analysis of the techniques and participated in the design and writing of the paper.

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REFERENCES

Andrew, J., and O'Riordan, T. (2004). "The precautionary principle: a legal and policy history," in *The precautionary principle: protecting public health, the environment and the future of our children*. Eds. M. Martuzzi and J. A. Tickner (Copenhagen: World Health Organization), 31–48. Available at: http://www.euro.who.int/__data/assets/pdf_file/0003/91173/E83079.pdf (Accessed December 1, 2019).

Antoniou, M. (2019). The EU must not de-regulate gene-edited crops and foods. *EURACTIV.com*. Available at: https://www.euractiv.com/section/agriculture-food/opinion/the-eu-must-not-de-regulate-gene-edited-crops-and-foods/ (Accessed August 10, 2019).

Beck, G. (2012). *The Legal Reasoning of the Court of Justice of the EU* (Kemp House, Chawley Park, Cumnor Hill, Oxford, OX2 9PH: Hart Publishing Limited).

Bioökonmierat (2018). *Press Release of 17 September 2018: "Genome editing: Germany"s Bioeconomy Council calls for new EU legislation". Berlin*, Available at: https://biooekonomierat.de/fileadmin/Pressemitteilungen/BO:R_GenomeEditing_PM_eng_final_2.pdf (Accessed December 1, 2019).

Blakeslee, A. F., and Avery, A. G. (1937). Methods of inducing doubling of chromosomes in plants: By Treatment With Colchicine. *J. Hered.* 28, 393–411. doi: 10.1093/oxfordjournals.jhered.a104294

Callaway, E. (2018). EU law deals blow to CRISPR crops. *Nature* 560, 16–16. doi: 10.1038/d41586-018-05814-6

Carlson, P. S., Smith, H. H., and Dearing, R. D. (1972). Interspecific Hybridization. *Encycl. Plant Crop Sci.* 69, 2292–2294. doi: 10.1081/e-epcs-120005682

CIOPORA (2018). Court of Justice of the European Union: Organisms Obtained by Mutagenesis are GMOs. *Public*. Available at: https://www.ciopora.org/single-post/2018/07/25/Court-of-Justice-of-the-European-Union-Organisms-Obtained-by-Mutagenesis-are-GMOs?mc_cid=f09679ffcc&mc_eid=d4aa1c30a2 (Accessed August 5, 2019).

CJEU (2018). Court of Justice of the European Union - PRESS RELEASE N° 111/18. *CURIA - Press Inf.* Available at: https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf (Accessed December 1, 2019).

Custers, R., Casacuberta, J. M., Eriksson, D., Sági, L., and Schiemann, J. (2019). Genetic alterations that do or do not occur naturally; Consequences for genome edited organisms in the context of regulatory oversight. *Front. Bioeng. Biotechnol.* 6, 213. doi: 10.3389/fbioe.2018.00213

Devuyst, P. (2018). ECJ ruling on new breeding techniques "creates more confusion", says MEP. *IEG Policy*. Available at: https://iegpolicy.agribusinessintelligence.informa.com/PL217772/ECJ-ruling-on-new-breeding-techniques-creates-more-confusion-says-MEP (Accessed May 17, 2019).

Dirks, R., Van Dun, K., De Snoo, C. B., Van Den Berg, M., Lelivelt, C. L. C., Voermans, W., et al. (2009). Reverse breeding: A novel breeding approach based on engineered meiosis. *Plant Biotechnol. J.* 7, 837–845. doi: 10.1111/j.1467-7652.2009.00450.x

Eriksson, D., Harwood, W., Hofvander, P., Jones, H., Rogowsky, P., Stöger, E., et al. (2018). A Welcome Proposal to Amend the GMO Legislation of the EU. *Trends Biotechnol.* 36, 1100–1103. doi: 10.1016/j.tibtech.2018.05.001

Eriksson, D. (2018). The Swedish policy approach to directed mutagenesis in a European context. *Physiol. Plant* 164, 385–395. doi: 10.1111/ppl.12740

Eskridge, W. N. (1987). Dynamic statutory interpretation. *Univ. PA Law Rev.* 135, 1479–1555. doi: 10.2307/3312014

European Union (2016). The precautionary principle. *EUR-Lex*. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=LEGISSUM%3Al32042 (Accessed November 30, 2019).

Gelinsky, E., and Hilbeck, A. (2018). European Court of Justice ruling regarding new genetic engineering methods scientifically justified: a commentary on the biased reporting about the recent ruling. *Environ. Sci. Eur.* 30, 52. doi: 10.1186/s12302-018-0182-9

Grimsley, N., Hohn, I., Hohn, T., and Waldent, R. (1986). 'Agroinfection,' an alternative route for viral infection of plants by using the Ti plasmid. *Proc. Natl. Acad. Sci. U.S.A.* 83, 3282–3286. doi: 10.1073/pnas.83.10.3282

Harašić, Ž. (2015). More about teleological argumentation in law. *Prav. Vjesn.* 3-4, 23–49. Available at: https://hrcak.srce.hr/file/229796 (Accessed December 1, 2019).

IAEA Mutant Variety Database - MVD. Available at: https://mvd.iaea.org/. (Accessed November 29, 2019).

IFOAM EU Group (2018a). *Press briefing: Preliminary ruling of the European Court of Justice on the legal status of plant breeding and genetic engineering techniques C-528*, (IFOAM EU Group, Söderköping, Sweden). Available at: https://www.ifoam-eu.org/sites/default/files/ifoameu_policy_kgoo_newgmos_pressbriefing_20180719.pdf (Accessed August 12, 2019).

IFOAM EU Group (2018b). *PRESS RELEASE: New genetic engineering techniques to be regulated as GMOS - IFOAM EU welcomes ECJ " s decision*, (IFOAM EU Group, Söderköping, Sweden). Available at: https://www.ifoam-eu.org/en/news/2018/07/25/press-release-new-genetic-engineering-techniques-be-regulated-gmos-ifoam-eu-welcomes (Accessed December 1, 2019).

IFOAM EU Group (2019). *All techniques of genetic modification must be regulated*, (IFOAM EU Group, Söderköping, Sweden). Available at: https://www.ifoam-eu.org/sites/default/files/ifoameu_policy_kgoo_newgmoleaflet_england_05062019.pdf (Accessed August 12, 2019).

IFOAM Organics International (2017). *Position Paper: Compatibility of Breading Techniques in Organic Systems*, (IFOAM Organics International, Bonn). Available at: https://www.ifoam.bio/sites/default/files/position_paper_v01_web_0.pdf (Accessed August 12, 2019).

Jiang, W., Zhou, H., Bi, H., Fromm, M., Yang, B., and Weeks, D. P. (2013). Demonstration of CRISPR/Cas9/sgRNA-mediated targeted gene modification in Arabidopsis, tobacco, sorghum and rice. *Nucleic Acids Res.* 41, 1–12. doi: 10.1093/nar/gkt780

Jorasch, P. (2016). How Much Plant Breeding Innovation is Politically Intended? *Eur. seed* 3. Available at: http://european-seed.com/much-plant-breeding-innovation-politically-intended/ (Accessed December 1, 2019).

Jorasch, P. (2019). "The view of the European seed sector on genome editing in plant breeding," in *1st PlantEd conference Plant Genome Editing - State of the Art: 5th – 7th November 2019 Novi Sad, Serbia* (Serbia: Novi Sad). Available at: https://plantgenomeediting.eu/wp-content/uploads/PlantEd-Conference-agenda_final.pdf (Accessed December 9, 2019).

Krämer, L. (2015). *Legal Questions Concerning New Methods for Changing the Genetic Conditions in Plants Commissioned by Arbeitsgemeinschaft Bäuerliche Landwirtschaft (Abl), Bund Für Umwelt Und Naturschutz (BUND), Bund Ökologische Lebensmittelwirtschaft (BÖLW), Etc*, Available At: http://Www.Testbiotech.Org/Sites/Default/Files/Kraemer_Legal Questions_New Methods_0.Pdf.

Leyser, O. (2018). GM crop ruling shows why the EU's laws are wholly inadequate. *Conversat*. Available at: https://theconversation.com/gm-crop-ruling-shows-why-the-eus-laws-are-wholly-inadequate-100675 (Accessed May 17, 2019).

Li, J. F., Norville, J. E., Aach, J., McCormack, M., Zhang, D., Bush, J., et al. (2013). Multiplex and homologous recombination-mediated genome editing in Arabidopsis and Nicotiana benthamiana using guide RNA and Cas9. *Nat. Biotechnol.* 31, 688–691. doi: 10.1038/nbt.2654

Lifschitz, E., Eviatar, T., Rozman, A., Shalit, A., Goldshmidt, A., Amsellem, Z., et al. (2006). The tomato FT ortholog triggers systemic signals that regulate growth and flowering and substitute for diverse environmental stimuli. *Proc. Natl. Acad. Sci.* 103, 6398–6403. doi: 10.1073/pnas.0601620103

Mandel, G. N. (2005). Technology Wars: Mending the Failure of Democratic Discourse. *SSRN Electron. J.* 11, 75. doi: 10.2139/ssrn.669142

Marks, S., and Livingstone, E. (2019). EU's top court tightens controls over controversial new GMO techniques – POLITICO. *Politico*. Available at: https://www.politico.eu/article/mutagenesis-genetically-modified-organisms-eu-court-opens-door-to-certain-contentious-plant-breeding-techniques/ (Accessed December 1, 2019).

Mendel, G. (1901). *Versuche Über Pflanzenhybriden: Zwei Abhandlungen, (1865 Und 1869)*. Ed. E. Tschermak (Leipzig: Verlang von Wilhelm Engelmann). doi: 10.1192/bjp.111.479.1009-a

Mercer, A. C., Gaj, T., Fuller, R. P., and Barbas, C. F. (2012). Chimeric TALE recombinases with programmable DNA sequence specificity. *Nucleic Acids Res.* 40, 11163–11172. doi: 10.1093/nar/gks875

Michalopoulos, S. (2018). Industry shocked by EU Court decision to put gene editing technique under GM law. *EURACTIV.com*. Available at: https://www.euractiv.com/section/agriculture-food/news/industry-shocked-by-eu-court-decision-to-put-gene-editing-technique-under-gm-law/ (Accessed December 1, 2019).

Michalopoulos, S. (2019). Andriukaitis: New plant breeding techniques need new regulatory framework. *EURACTIV.com*. Available at: https://www.euractiv.com/section/agriculture-food/news/andriukaitis-new-plant-breeding-techniques-need-new-regulatory-framework/ (Accessed August 6, 2019).

New Techniques Working Group (2012). *Final Report* (European Commission). Available at: http://www.seemneliit.ee/wp-content/uploads/2011/11/esa_12.0029.pdf (Accessed December 1, 2019).

Noisette, C. (2019). L'arrêt de la Cour européenne sur les « nouveaux OGM » attaqué. *info'OGM Veill. citoyenne d'information sur les OGM les semences*. Available at: https://www.infogm.org/spip.php?page=spipdf&spipdf=spipdf_article&id_article=6754&nom_fichier=infogm-article-6754 (Accessed August 6, 2019).

Opoku Gakpo, J. (2018). The Netherlands: EU ruling on new breeding techniques could harm seed exports. *Cornell Alliance Sci*. Available at: https://allianceforscience.cornell.edu/blog/2018/10/netherlands-eu-ruling-new-breeding-techniques-harm-seed-exports/ (Accessed December 2, 2019).

Piatek, A., Ali, Z., Baazim, H., Li, L., Abulfaraj, A., Al-Shareef, S., et al. (2015). RNA-guided transcriptional regulation in planta *via* synthetic dCas9-based transcription factors. *Plant Biotechnol. J.* 13, 578–589. doi: 10.1111/pbi.12284

Purnhagen, K. P., Kok, E., Kleter, G., Schebesta, H., Visser, R. G. F., and Wesseler, J. (2018a). EU court casts new plant breeding techniques into regulatory limbo. *Nat. Biotechnol.* 36, 799–800. doi: 10.1038/nbt.4251

Purnhagen, K. P., Kok, E., Kleter, G., Schebesta, H., Visser, R. G. F., and Wesseler, J. (2018b). The European Union Court's Advocate General's Opinion and new plant breeding techniques. *Nat. Biotechnol.* 36, 573–575. doi: 10.1038/nbt.4174

Reich, T. J., Iyer, V. N., and Miki, B. L. (1986). Efficient transformation of alfalfa protaplasts by the intranuclear microinjection of Ti plasmids. *Biotechnology*, 4, 1001–1004. doi: 10.1038/nbt1186-1001

Rösler, H. (2012). Interpretation of EU law. *Max Planck Encycl. Eur. Priv. Law* 2, 979–982. Available at: http://www.newbooks-services.de/MediaFiles/Texts/5/9780199578955_Excerpt_001.pdf (Accessed December 2, 2019).

Rommens, C. M., Haring, M. A., Swords, K., Davies, H. V., and Belknap, W. R. (2007). The intragenic approach as a new extension to traditional plant breeding. *Trends Plant Sci.* 12, 397–403. doi: 10.1016/j.tplants.2007.08.001

Ruiz-Ferrer, V., and Voinnet, O. (2009). Roles of Plant Small RNAs in Biotic Stress Responses. *Annu. Rev. Plant Biol.* 60, 485–510. doi: 10.1146/annurev.arplant.043008.092111

Sadeleer, N. de (2014). *EU environmental law and the internal market* (Oxford, UK: Oxford University Press). Available at: https://global.oup.com/academic/product/eu-environmental-law-and-the-internal-market-9780199675432?cc=us&lang=en&.

Salvi, L. (2016). The EU Regulatory Framework on GMOs and the Shift of Powers towards Member States: an Easy Way Out of the Regulatory Impasse? *Eur. Food Feed Law Rev.* 11, 201–210. doi: 10.2307/90008660

SAM (2017). *New technologies in agricultural biotechnology: High Level Group of Scientific Advisors: Explanatory Note 02/2017* (Brussels: European Commission). doi: 10.19040/ecocycles.v2i2.65

SAM (2018). *Statement by the Group of Chief Scientific Advisors: A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive* (Brussels: European Commission). Available at: https://ec.europa.eu/info/sites/info/files/2018_11_gcsa_statement_gene_editing_1.pdf (Accessed December 2, 2019).

Scholz, L., and Cunha, E. (2017). Historical Interpretation. *Wikis der Freien Univ. Berlin*. Available at: https://wikis.fu-berlin.de/display/oncomment/Historical+Interpretation (Accessed August 13, 2019).

Scholz, L. (2012a). Contextual interpretation. *Wikis der Freien Univ. Berlin*. Available at: https://wikis.fu-berlin.de/display/oncomment/Contextual+Interpretation (Accessed August 13, 2019).

Scholz, L. (2012b). Teleological Interpretation. *Wikis der Freien Univ. Berlin*. Available at: https://wikis.fu-berlin.de/display/oncomment/Teleological+Interpretation (Accessed August 13, 2019).

Schouten, H. J., Krens, F. A., and Jacobsen, E. (2006). Do cisgenic plants warrant less stringent oversight? [6]. *Nat. Biotechnol.* 24, 753. doi: 10.1038/nbt0706-753

Science Media Centre (2018). expert reaction to Court of Justice of the European Union ruling that GMO rules should cover plant genome editing techniques. *roundups journalists*. Available at: https://www.sciencemediacentre.org/expert-reaction-to-court-of-justice-of-the-european-union-ruling-that-gmo-rules-should-cover-plant-genome-editing-techniques/ (Accessed December 2, 2019).

Shan, Q., Wang, Y., Li, J., Zhang, Y., Chen, K., Liang, Z., et al. (2013). Targeted genome modification of crop plants using a CRISPR-Cas system. *Nat. Biotechnol.* 31, 686–688. doi: 10.1038/nbt.2650

Sharma, D. R., Kaur, R., and Kumar, K. (1996). Embryo rescue in plants - A review. *Euphytica* 89, 325–337.

Shi, J., Gao, H., Wang, H., Lafitte, H. R., Archibald, R. L., Yang, M., et al. (2017). ARGOS8 variants generated by CRISPR-Cas9 improve maize grain yield under field drought stress conditions. *Plant Biotechnol. J.* 15, 207–216. doi: 10.1111/pbi.12603

Shmakov, S., Abudayyeh, O. O., Makarova, K. S., Wolf, Y. I., Gootenberg, J. S., Semenova, E., et al. (2015). Discovery and Functional Characterization of Diverse Class 2 CRISPR-Cas Systems. *Mol. Cell* 60, 385–397. doi: 10.1016/j.molcel.2015.10.008

Spranger, T. M. (2015). *Legal Analysis of the applicability of Directive 2001/18/EC on genome editing technologies commissioned by the German Federal Agency for Nature Conservation* (Bonn: German Federal Agency for Nature Conservation).

Sprink, T., Eriksson, D., Schiemann, J., and Hartung, F. (2016). Regulatory hurdles for genome editing: process- vs. product-based approaches in different regulatory contexts. *Plant Cell Rep.* 35, 1493–1506. doi: 10.1007/s00299-016-1990-2

Stadler, L. J. (1928). Mutations in barley induced by x-rays and radium. *Science* 68, 186–187. doi: 10.1126/science.68.1756.186

The Irish Times (2019). Plants using new gene-editing methods must comply with EU directives on GMOs - ECJ. *Irish Times*. Available at: https://www.irishtimes.com/business/agribusiness-and-food/plants-using-new-gene-editing-methods-must-comply-with-eu-directives-on-gmos-ecj-1.3576354 (Accessed December 2, 2019).

Urnov, F. D., Ronald, P. C., and Carroll, D. (2018). A call for science-based review of the European court's decision on gene-edited crops. *Nat. Biotechnol.* 36, 800–802. doi: 10.1038/nbt.4252

Vives-Vallés, J. A. (2016). *Derecho de Cultivos Transgénicos: El conflicto entre el Derecho español y comunitario y el derecho a la libertad de empresa, a la luz de la nueva normativa opt-out* (Madrid: Dykinson).

Vives-Vallés, J. A. (2018). Coexistencia entre maíz transgénico y convencional: análisis integral y propuesta de criterios técnicos para las Illes Balears. *University of the Balearic Islands, Palma* p. 410.

Wanner, B., Monconduit, H., Mertens, A., and Thomaier, J. (2019). CJEU renders decision on the interpretation of the GMO Directive. *J. Intellect. Prop. Law Pract.* 14, 90–92. doi: 10.1093/jiplp/jpy184

Weimer, M. (2019). *Risk regulation in the internal market : lessons from agricultural biotechnology* (Oxford, UK: Oxford University Press). doi: 10.1093/oso/9780198732792.001.0001 Available at: https://global.oup.com/academic/product/risk-regulation-in-the-internal-market-9780198732792?cc=us&lang=en&.

Woo, J. W., Kim, J., Kwon, S. Il, Corvalán, C., Cho, S. W., Kim, H., et al. (2015). DNA-free genome editing in plants with preassembled CRISPR-Cas9 ribonucleoproteins. *Nat. Biotechnol.* 33, 1162–1164. doi: 10.1038/nbt.3389

Zambryski, P., Joos, H., Genetello, C., Leemans, J., Van Montagu, M., and Schell, J. (1983). Ti plasmid vector for the introduction of DNA into plant cells without alteration of their normal regeneration capacity. *EMBO J.* 2, 2143–2150. doi: 10.1002/j.1460-2075.1983.tb01715.x

Zhu, T., Peterson, D. J., Tagliani, L., St. Clair, G., Baszczynski, C. L., and Bowen, B. (1999). Targeted manipulation of maize genes *in vivo* using chimeric RNA/DNA oligonucleotides. *Proc. Natl. Acad. Sci. U. S. A.* 96, 8768–8773. doi: 10.1073/pnas.96.15.8768

Zimmere, C. (2018). *What Is a Genetically Modified Crop? A European Ruling Sows Confusion* (The New York Times, New York). Available at: https://www.nytimes.com/2018/07/27/science/gmo-europe-crops.html (Accessed December 2, 2019).

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Do New Breeding Techniques in Ornamentals and Fruits Lead to Essentially Derived Varieties?

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Do new breeding techniques (NBT) lead to essentially derived varieties (EDV)? It depends! It depends on the definition of EDV in the plant variety right (PVR) laws and their interpretation by the courts. This paper aims at providing an overview of the EDV concept and an analysis of the question whether NBT lead to EDV on the basis of the UPOV 1991 Act, the most recent UPOV Explanatory Notes on EDV of 2017 as well as some selected PVR laws. Almost 30 years ago, the concept of EDV has been incorporated into the UPOV 1991 Act. In order to strengthen the rights of breeders, in particular to provide breeders of original genotypes an additional source of remuneration, a system of "Plant Variety Right specific dependency," based on "essential derivation," was developed. Only a very limited number of court cases have been concerned with EDV. However, an escalation in EDV-related conflicts can be expected in the future due to increased competition in the ornamental and fruit breeding business as well as to the application of more sophisticated NBT.

Keywords: plant breeder's right, essentially derived varieties, new breeding techniques, UPOV Convention, mutants, fruits, ornamental plants

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INTRODUCTION

Almost 30 years ago, the concept of essentially derived varieties has been incorporated into the UPOV 1991 Act. In order to strengthen the rights of breeders [UPOV (1989), Introduction, chapter B. 5. (i)], in particular to provide breeders of original genotypes an additional source of remuneration [UPOV (1989), p. 12, No. 6. (iii)], a system of "Plant Variety Right specific dependency (Leßmann, 2000)," based on "essential derivation," was developed.

Incorporating the EDV concept meant a true extension of the breeder's rights. The right of the breeder to exclude others from specific acts such as producing, selling, exporting, and importing no longer covers only the protected variety itself, but also varieties that are essentially derived from the protected variety. Thus, the principle of EDV involves questions of the scope of the breeder's rights and its infringement. It is therefore left to the initiative of the breeders to enforce their rights[1].

Until now, the EDV concept has been included in the Plant Variety Right laws of 65 UPOV member states, 7 of them being party only to the UPOV 1978 Act[2]. Unfortunately, the Plant Patent Act

[1] A different approach is—yet—followed by Australia. Australia is—as far as can be seen—the only UPOV member state where the PVR authorities play an active role in the declaration of a new variety to be or not to be an EDV.
[2] Bolivia, Brazil, Colombia, Ecuador, Italy, Nicaragua, and South Africa.

of the United States, the basic and most widely used regulation for the protection of intellectual property of ornamental and fruit breeders in the U.S., does not yet contain a provision on EDV[3].

Several publications about EDV have been issued[4]. Only a very limited number of court cases have been concerned with EDV[5], apparently due to the fact that breeders are hesitant to start court proceedings due to the complexity of the matter and the ambiguous provisions of the applicable plant variety right (PVR) laws. Additionally, breeders seem to be more careful in their breeding programs in order to avoid possible EDV cases. At least in the US (ASTA) and France (SEPROMA), for maize, different zones (red, orange, green) have been agreed upon when dealing with pairwise genetic distances between potential initial and essentially derived varieties based on molecular marker profiles. It has become part of the arbitration system but is also used in practice to keep away from breeding too close to a competitor's genetic material (UPOV-BMT reports, available on https://www.upov.int/portal/index.html.en).

However, an escalation in EDV-related conflicts can be expected in the future due to increased competition in the ornamental and fruit breeding business as well as to the application of more sophisticated "breeding" methods, the so-called new breeding techniques (NBT). In ornamentals and fruits, one is typically dealing with long breeding times that can reach up to 20 years. However, mutations into these crops are easily detected when propagated on larger scales and can immediately be introduced into the market. By use of NBT, targeted development of innovative EDV can become a very attractive and fast route to new varieties. Different to seed propagated species where the owner of a variety often also controls the propagation and final marketing of the seeds, vegetative species are in a way "free" and have to rely on a stronger IP protection system. The PBR system in Europe is seen by the sector as one of the most performant systems, and this results into a high number of applications in ornamental and fruit crops (**Figure 1**) (CPVO, 2018).

In the United States, two main IP systems are used for the protection of plant Fi varieties: Plant Patents for the asexually reproduced plants (other than tuber-propagated) and Plant Breeders´ Rights for the seed propagated crops[6] (**Figure 2**). Over the past 5 years, twice as many applications were filed for Plant Patents than Plant Breeders' Rights in the U.S. (**Figure 3**) demonstrating the significance of IP protection for asexually reproduced species.

According to the High Level Group of Scientific Advisors (2017), the term NBT describes a very diverse range of techniques, some of which are substantially different from established transgenic approaches in their way of introducing traits to an organism (EASAC, 2015). Some are a refinement of conventional breeding techniques and insert genetic material that is derived from a sexually compatible species, while some nevertheless are used in combination with established techniques of genetic modification. Some of the NBT result in organisms that contain only point mutations and are practically indistinguishable from varieties bred through conventional breeding methods or resulting from spontaneous mutations (EASAC, 2015). In this paper we focus on NBTs (as listed by the EU and in detail explained by the High Level Group of Scientific Advisors, 2017), but explicitly not including "grafting" and "agro-infiltration," as the resulting products of these above defined NBTs are most similar to conventional mutagenesis and genetic modification.

THE TEXT OF THE UPOV 1991 ACT REGARDING EDV

The starting point of this discussion about EDV is the text of the UPOV 1991 Act. However, it must first be noted that the UPOV 1991 Act, like any other UPOV Act, does not have a direct effect in the UPOV member states. The UPOV Act only sets the minimum requirements of PVR laws in the UPOV member states. The legal basis for EDV are the specific PVR laws on which the PVR title and the EDV-claim are based. In many cases, the wording of the provisions dealing with EDV of such PVR laws differs significantly from the wording of the UPOV 1991 Act[7]. However, it is solely the provisions of the applicable PVR laws that govern the legal relationship of those involved. Only when there are incomplete or inconclusive provisions that give room for interpretation, the UPOV text may be consulted. In this regard, UPOV has since 2008 drafted two explanatory notes (EXN) on EDV, which aim at providing guidance and assist members of UPOV and relevant stakeholders in their consideration in matters concerning EDV (UPOV, 1992; UPOV, 2017). The most recent one is the EXN on EDV approved in April 2017. However, it should be noted that the EXN is not binding for UPOV members and must not be interpreted in a way that is inconsistent with the relevant UPOV Act.

The sections regarding EDV can be found mainly in Article 14 (5) (a) (i), (b), and (c) of the UPOV 1991 Act. They have to be read in the context of the complete Article 14 (Scope of the Breeders´ Rights), in which the provisions have been incorporated. Additionally, Article 15 (1) (iii) also contains an important link to EDV.

[3] Since 2018 the US Plant Variety Protection Act is open for vegetatively reproduced crops, too, so that the breeders of such crops can benefit from the EDV Concept in the USA, too.

[4] See list of literature at the end of the article for Crespel et al. (2009), Hunter (1999), Korzun and Heckenberger (2004), Lange (1993), Vosman et al. (2004) and Zhang et al. (2001).

[5] The Court of Civil Law in The Hague, The Netherlands (File-No. 2003/1054) on 13 July 2005 has issued a decision in a case concerned with Gypsophila and denied the existence of an EDV, the Tel Aviv-Jaffa District Court, Israel (File - No.002002/05) on 21 September 2005 approved for the same variety the existence of an EDV. See also Turin Trial Court, File-No GR No 28969/2009, Judgment No 3519/2015 published on 14/05/2015, Regional Court of Mannheim, decision 7 O 442/04.

[6] Since 2019 asexually reproduced crops can also be protected by Plant Breeders´ Rights—driven by the missing EDV concept in the Plant Patent Act. Additionally, varieties can be protected by Utility Patents in the US, too, but this was not common practice for asexually reproduced crops in the past.

[7] The majority of the 65 member states of UPOV with an EDV provision have strictly copied the UPOV text on EDV. A prominent example for a different wording is the European PVR-Regulation 2100/94.

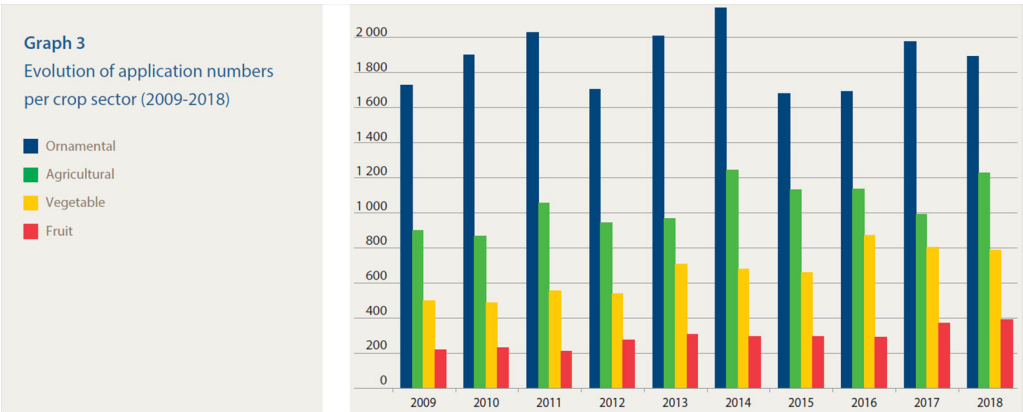

FIGURE 1 | Evolution of PBR-application numbers per crop sector (2009–2018) at the CPVO (2018).

Article 14
Scope of the Breeder's Right
(1) [*Acts in respect of the propagating material*]
(2) [*Acts in respect of the harvested material*]
(3) [*Acts in respect of certain products*]
(4) [*Possible additional acts*]
(5) [*Essentially derived and certain other varieties*]
(a) The provisions of paragraphs (1) to (4) shall also apply in relation to
(i) varieties which are essentially derived from the protected variety, where the protected variety is not itself an essentially derived variety,
(ii) varieties which are not clearly distinguishable in accordance with Article 7 from the protected variety and
(iii) varieties whose production requires the repeated use of the protected variety.
(b) For the purposes of subparagraph *(a)* (i), a variety shall be deemed to be essentially derived from another variety ("the initial variety") when
(i) it is predominantly derived from the initial variety, or from a variety that is itself predominantly derived from the initial variety, while retaining the expression of the essential characteristics that result from the genotype or combination of genotypes of the initial variety,
(ii) it is clearly distinguishable from the initial variety and
(iii) except for the differences which result from the act of derivation, it conforms to the initial variety in the expression of the essential characteristics that result from the genotype or combination of genotypes of the initial variety.
(c) Essentially derived varieties may be obtained for example by the selection of a natural or induced mutant, or of a somaclonal variant, the selection of a variant individual from plants of the initial variety, backcrossing, or transformation by genetic engineering.

Article 15
Exceptions to the Breeder's Right
(1) [*Compulsory exceptions*] The breeder's right shall not extend to
(i) acts done privately and for non-commercial purposes,
(ii) acts done for experimental purposes and
(iii) acts done for the purpose of breeding other varieties, and, except where the provisions of Article 14 (5) apply, acts referred to in Article 14 (1) to (4) in respect of such other varieties.

THE BASICS OF "BREEDER'S EXEMPTION" AND "DEPENDENCY" AND THE HISTORICAL BACKGROUND AND MOTIVES FOR INCORPORATING THE EDV-CONCEPT INTO THE UPOV 1991 ACT

Free Access to Germplasm

From the very first day of the UPOV-system, starting with the UPOV 1961 Act, the principle of free access of breeders to existing breeding material (genotypes/germplasm) for the purpose of breeding new varieties has been established. The main reason for having included and maintained this principle through the UPOV Acts is that any breeding is based on existing living material and thus breeders have to depend on free access to different genotypes to avoid a concentration on only a very limited number of varieties (Leßmann, 2000). The majority of breeders and their associations support this principle of free access to germplasm (see CIOPORA).

This is a fundamental element of the UPOV system of plant variety protection known as the "breeder's exemption," whereby there are no restrictions on the use of protected varieties for the purpose of breeding new plant varieties. The authorization of the breeder for the use of protected varieties for breeding purposes is

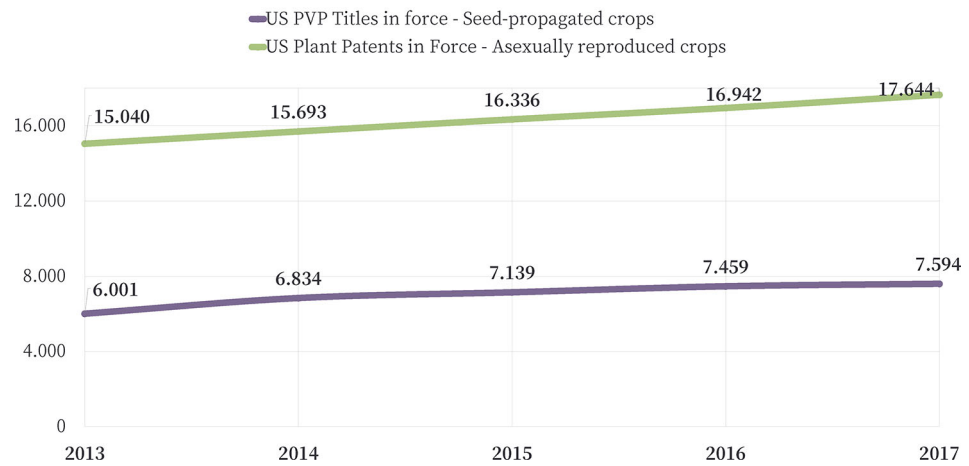

FIGURE 2 | Evolution of the U.S. Plant Variety Rights (PVP) vs. U.S. Plant Patents in force in each consecutive year (2013–2017). Source: UPOV, 2019.

required neither under the 1978 Act nor under the 1991 Act. The Breeder's Exemption also permits the application of NBT on protected varieties.

There is no such concept of breeder's exemption in the patent system under the European Patent Convention (EPC) although it has been implemented in some national patent laws. Still breeders also take into account patent protection because of the innovations involving technical solutions to develop new varieties. Under the current European patent protection, which is a stronger and more absolute protection than PVR in respect of the strict substantial requirements examination and its scope of exclusive rights, any use of the patented products (e.g. genetic material) and processes covered by the patent must obtain permission from the patent owner. This blocks access to biological materials for further breeding.

The Shortcomings of the Overly Broad "Breeder's Exemption" in the Past

Compared to the position of a patent holder as described before, the position of breeders with regard to the scope of protection was weak before the revision of the UPOV Act in 1991. Additionally, too many loopholes where found in the individual PVR laws. In particular the broad wording of the "breeder's exemption" combined with the absence of adequate provisions on the control of varieties that are very similar compared to a protected variety left the door wide open to so called "cosmetic breeding" and plagiarism. In addition, the situation regarding "mutants" was not satisfactorily covered by the PVR laws, as the breeders of the original varieties were unable to control said mutants. Even by way of license-agreements, an adequate control could not be reached (decision of the European Commission, 1985).

Mutants and New Bio-Technologies as the Initial Point for the EDV-Concept

Therefore, it was mainly the breeders of vegetatively reproduced crops, namely ornamental and fruit plants, who were dissatisfied with the fact that third parties, due to the limited scope of protection of the preceding UPOV Acts, were allowed to exploit and even acquire PVR protection for mutants of protected varieties without the original breeder being able to participate in the use and exploitation of these mutants (Kiewiet, 2002). Mutants play a significant role in many ornamental species. As estimated by breeding companies, many of important ornamental varieties are mutants:

In addition, it was the development of GMO technologies which enables adding new characteristics to existing varieties by way of biotechnological methods that led to the introduction of the concept of dependent plant variety rights. Conventional breeders were concerned that such new GMO varieties could be used without them receiving any financial compensation for the use of the germplasm they have created through conventional breeding methods.

This discussion has gained momentum again in the recent past with the advent of NBT. Conventional GMO have not been applied in ornamentals and fruits a lot due to high costs of regulatory issues and companies not willing to put their reputation at risk. Mutagenesis on the contrary has yielded more than 3,200 novelties, some of them well known like the orange flesh grapefruit (Source FAO/IAEA Mutant Varieties Database: https://mvd.iaea.org/). NBT also allow to develop a trait in a parental line that can be quickly introgressed by backcrossing into an existing variety. In species with a short commercial life, like lettuce and other vegetables, this new phenomenon might lead to even more closely related varieties. Again, the fear is raised that an NBT variety could easily take

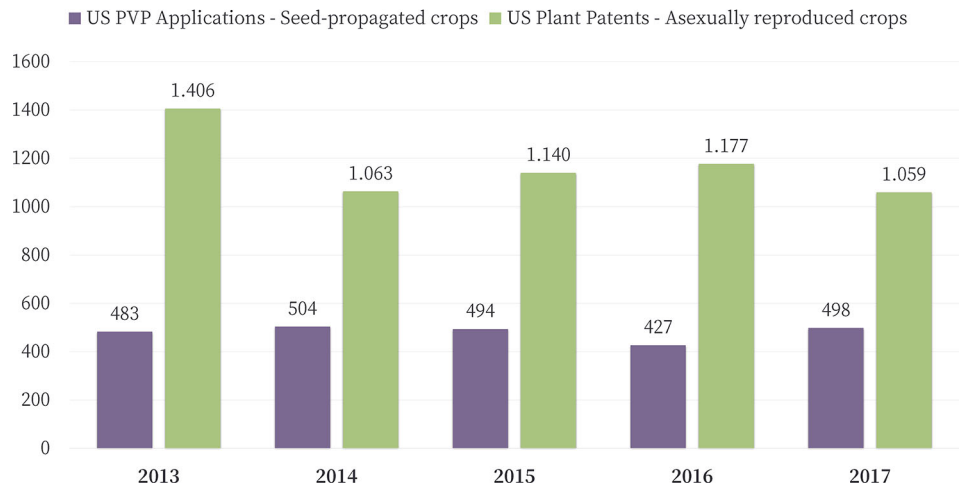

FIGURE 3 | Evolution of the U.S. Plant Variety Rights (PVP) vs. U.S. Plant Patent applications (2013–2017). Source: UPOV, 2019.

over the market when an innovative feature is added onto a conventionally bred variety.

ANALYSIS OF THE EDV-CONCEPT

Systematic Framework

The EDV clause is included in Article 14 of the UPOV 1991 Act ("Scope of the Breeder's Right"). This shows that the EDV concept is part of the scope of the right and not an exception or limitation, like those provisions of Article 15 of the 1991 Act.

However, the EDV Concept is a limitation in another sense: According to Article 15 (1) (iii) *the breeder's right shall not extend to acts done for the purpose of breeding other varieties, and, except where the provisions of Article 14 (5) apply, acts referred to in Article 14 (1) to (4) in respect of such other varieties (Breeder's´ exemption)*. In other words: Acts for the purpose of breeding a new variety are always allowed without the consent of the breeder of the initial variety, but the exploitation of such a new variety is allowed only as long as the new variety is not considered to be an EDV. In that way the EDV Concept is indeed a limitation of the breeders´ exemption, not in respect of the free access to germplasm, but in respect of the commercialization of the newly developed variety, if this is an EDV.

"Classical Breeding Work" in the EDV Concept

The term "classical breeding work"[8] is one of the keywords in the EDV concept. The term first leads to a discussion on the contradiction between the definition of "breeder" in Article 1 (iv) of the UPOV 1991 Act and the "classical breeding work" in the framework of the EDV concept. Whereas according to Article 1 (iv) of the UPOV 1991 Act both, i.e., those who "cross and select" as well as those who "discover and develop," new varieties deserve the title "breeder," in the EDV-concept "classical breeding" only means the crossing of parental varieties and the selection of the resulting progenies with the aim to create new variations. The definition of a "breeder" mainly results from the purpose of the UPOV 1991 Act to be applied also to a variety originating from a mutation (see UPOV, 1991). However, although UPOV does not differentiate between "classical breeding work" a "discovering and developing" on the level of the definition of the term "breeder," UPOV nevertheless sets apart the "classical breeding work", as only the results of such "classical breeding work" shall benefit from the EDV concept and from the extension of the scope of rights. The reason for this is that huge personal and financial endeavors have to be made to create new varieties by way of such "classical breeding".

In many parts of the world, breeders are often small and medium-sized companies. Until now they mostly breed innovative varieties in a conventional way by crossing and selection, which can take up to 20 years of hard work. Breeding innovative varieties in a conventional way is one of the backbones of the ornamental and fruit industries. It requires significant human and financial investment to develop such varieties. In order to guarantee a sustainable continuation of such breeding there needs to be a sufficient return on investment. Only varieties that are the result of classical breeding work qualify for the extended protection provided by the EDV concept.

The Conditions of an EDV

The Initial Variety (Article 14 (5) (a) (i) UPOV 1991 Act)

The initial variety forms the basis of any EDV claim. It derives from the principle of dependency that the initial variety must enjoy PVR

[8] Or "true breeding work" as used in UPOV (1989).

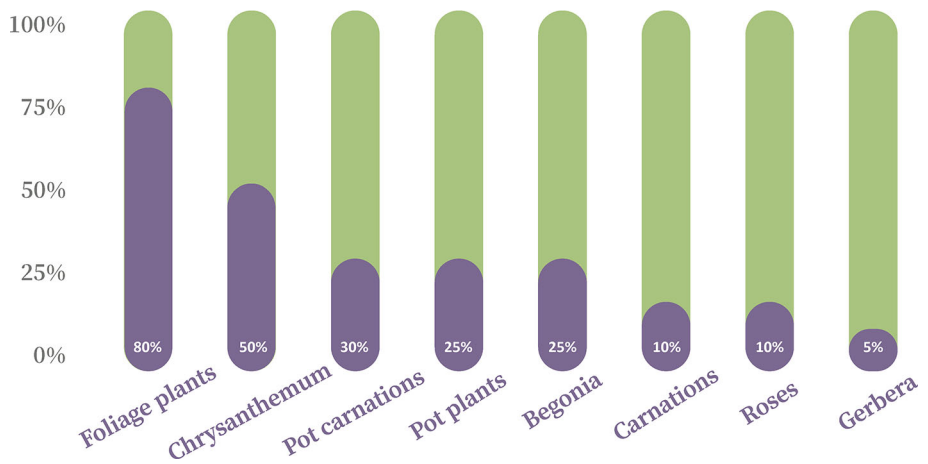

FIGURE 4 | Market shares of color mutants in ornamentals as estimated by breeders, 2019.

protection or at least provisional protection according to Article 13 of the UPOV 1991 Act. Therefore, in general the dependency of an essentially derived variety starts with the beginning of the provisional protection of the initial variety and ends with the end of protection of the initial variety (either by expiration or cancellation). Additionally, the initial variety cannot itself be an EDV. Although by introducing the EDV concept a certain degree of dependency has been created, so called "dependency pyramids" were to be avoided. The initial variety, therefore, must be the result of "classical breeding work" [UPOV, Doc. IOM/IV/2, page 12, No. 6 (iv)]. As already mentioned before, essential derivation is a matter of fact. Therefore, an EDV remains an EDV forever. Even if the protection period of the initial variety is exhausted, all varieties derived from this initial variety will still be essentially derived from the initial variety, but not *dependent* of the initial variety which is no longer protected. The reason for this is that the EDV-concept has mainly been introduced to protect more efficiently the breeder of the initial variety and not those who make derivations from his work (see also International Seed Federation, 2005).

Clearly Distinguishable

The EDV has to be *clearly distinguishable* from the initial variety. This requirement draws the line between an EDV and a variety which is not clearly distinguishable from the protected variety in the meaning of Article 14 (5) (a) (ii) in combination with Article 7 UPOV 1991 Act (see UPOV, 2017). Whereas the EDV is a discrete variety which is in principle eligible for PVR protection[9], a variety not clearly distinguishable from the protected variety is not a discrete one and cannot enjoy separate PBR protection but falls automatically within the scope of the earlier protected variety.

Some claim that the EDV concept aims at preventing plagiarism. However, in our view plagiarism is not a question of derivation or dependency, but rather a question of Minimum Distance/Distinctness and direct infringement. If a variety in its phenotype very much resembles a protected variety, it is not clearly distinguishable from the protected variety, and its commercialization is a direct infringement, irrespective whether the new variety is (essentially) derived from the protected variety or not. Instead, the fact that an EDV needs to be distinct from its Initial Variety makes it clear that a plagiaristic variety can never be regarded as EDV, as a plagiaristic variety already lacks the Distinctness. Declaring plagiaristic varieties as EDV would have the strange consequence that PBR Offices would be forced to grant Plant Breeders´ Rights titles to plagiaristic varieties, because EDV in principle are eligible for PVR protection.

The application of NBT usually will result in varieties which are clearly distinguishable from their Initial Variety. In fact, such varieties usually would not aim at copying an existing variety but adding an important or innovative trait to the initial variety. NBT are in principle not plagiaristic.

Predominant Derivation

The second condition an EDV will have to fulfil as stipulated by the UPOV 1991 Act is that it is *predominantly derived* from the initial variety or, as the case may be, from a variety that itself is *predominantly derived* from the initial variety. Predominant derivation relates to the genetic origin of the variety.

The first and in the field of vegetatively reproduced ornamental and fruit varieties by far the most important group of EDV are so called mono-parental varieties, like mutations, that are not only

[9] If it meets the additional criteria (novelty, uniformity and stability).

predominantly, but totally derived from their mother-variety. The importance of this group of varieties is mirrored by the examples given as acts of "derivation" in Article 14 (5) (c) UPOV 1991 Act. Four of the examples listed in the UPOV Act, i.e., mutants, somaclonal variants, variant individuals from plants of the initial variety, and genetically modified plants (GMO) resulting from transformation by genetic engineering, are mono-parental varieties. A mono-parental variety has its basis in one genome only (the genome of the initial variety), which was altered by the acts of derivation mentioned before. The half-sentence "while retaining the expression of the essential characteristics that result from the genotype or combination of genotypes of the initial variety" indicates that predominantly derived varieties essentially retain the expressed characteristics of the initial protected variety but does not stipulate an additional requirement for predominant derivation. The meaning of this sentence is further limited by (iii): "except for the differences which result from the act of derivation."

For NBT varieties the condition of predominant derivation is fulfilled, because NBT varieties—like mutants—are mono-parental varieties, solely derived from their Initial Variety. Even if by way of the NBT multiple changes are made to the genome of the initial variety (stacking), the new variety is based solely on the genome of the initial variety and the genetic conformity will be very high.

Conformity to the Initial Variety

The main dispute in regard to EDV is about the alleged requirement of conformity of the EDV compared to its Initial Variety. A judgment on the question on the degree of conformity must be reached on the basis of the expression of characteristics which result from the genotype of the initial variety. This judgment has to assess the conformity to the description of the initial variety apart from the specific differences which result from such breeding methods and other minimal differences which result incidentally from such breeding methods, such differences being evidenced at the level of the genome, the genotype or the phenotype. Article 14(5)(b)(iii) does not set a limit to the amount of difference which may exist where a variety is considered to be essentially derived. Differences, which result from the act of derivation, shall not be taken into consideration for the determination of an EDV.

Voices in literature are of the opinion that only varieties that show one or, at the most, a very limited number of phenotypic differences, can be considered as EDV (without reasoning, van der Kooij (1997), Introduction to the EC Regulation on Plant Variety Protection, Art. 13 (5) EC Regulation 2100/94, page 32; Court of Civil Law in The Hague, footnote 8, which based this opinion on its interpretation of the term "essentially derived" in indent (i) of Article 14 (5) (b) UPOV 1991 Act and UPOV document IOM/IV/2, page 12, No. 6 (ii), without considering the later UPOV Doc IOM/6/2. In an even more narrow interpretation, the UPOV EXN on EDV of 2017 states that a variety cannot be predominantly derived if it does not retain the essential characteristics of the initial variety [see UPOV (2017)]. This sentence is interpreted in a way that a variety can be considered to be an EDV only if it retains all essential characteristics of its Initial Variety. The EXN follows the very narrow Australian approach on EDV, where the Australian PBR Office declares a variety as EDV only if it differs in an unessential characteristic from the Initial Variety (see presentation of Australia in UPOV EDV Seminar 2013, https://www.upov.int/edocs/mdocs/upov/en/upov_sem_ge_13/upov_sem_ge_13_ppt_9.pdf).

We do not agree to this approach. Already the wording of Article 14 (5) (a) (ii) shows that this argument is not cogent. The condition "clearly distinguishable" according to Article 7 of the UPOV 1991 Act requires at least one "clear" difference between the EDV and the initial variety, whereas in several cases even one difference is not enough to consider one variety "clearly" distinguishable from another [see e.g. Article 5.3.3.2.1 of the UPOV document TG 1/3 "General Introduction to the Examination of Distinctness, Uniformity and Stability and the Development of Harmonized Descriptions of new Varieties of Plants" https://www.upov.int/tgp/en/introduction_dus.html)].

The narrow interpretation of the EDV-concept in allowing only one or fewer differences between the initial variety and its EDV disregards the new tendencies in the development of new varieties, because certain methods of developing new varieties, applying chemicals and other mutagens or NBT, allow the development of plants which differ considerably from the mother plant without altering the genome of the plant significantly. In fact, depending on the act of derivation the number of differing phenotypic characteristics between the initial variety and the variety derived thereof can differ significantly, between one, a few or even numerous. For example, mitotic polyploids express in general an increased size in all plant organs and an intensification of physiological characters. Such increases in plant organs can easily lead to numerous different characteristics as described in the test guidelines provided for by UPOV.

Additionally, requiring that an EDV must retain all essential characteristics of the Initial Variety would make the EDV Concept meaningless to a huge extent. A flower color-mutant in an ornamental variety is one typical case of an EDV. The characteristic "colour" can be regarded as one of the most if not the most important characteristics in ornamental varieties (**Figure 4**), presumably an *essential* characteristic. The colour-mutant clearly does not retain the essential characteristic "colour" of the initial variety and thus could not be considered an EDV, although being a mutant, is *the* typical example of an EDV and has been one of the main reasons for the introduction of the EDV-concept[10].

Also varieties resulting from NBT do in principle not retain all essential characteristics of their Initial Varieties, because the NBT have been deliberately applied with the aim to change essential characteristics of the initial variety, e.g. by introducing a resistance into a susceptible variety or to limit the browning of apples ("Arctic Apple", https://www.arcticapples.com/). According to the narrow UPOV EXN on EDV of 2017 and the Australian approach (Government of Australia, 2002), such NBT

[10] In fact, there are voices which deny the existence of an EDV in such case, see the citation of Kiewiet (2002) in: Plant Variety Rights in a community context, page 5, Opposite to this, the case of a colour mutation is listed as one example of an EDV in the brochure of the Japanese PVR office explaining the PVR system in Japan.

varieties would not be considered EDV. However, against the background that the NBT variety consists almost entirely of the genome of the initial variety, it seems highly unfair to the breeder of the initial variety to deprive him of any benefit from the NBT. Additionally, if the New Breeding Technology is protected by a Patent, the Patent holder can prevent the breeder of the initial variety from commercializing his variety or even to further breed with it. In order to prevent such a situation (in 1991 with a focus on GMO), the EDV Concept was established.

The narrow approach of the UPOV EXN on EDV is based on the last half sentence of indent (i) of Article 14 (5) (b) of the UPOV 1991 Act, which reads:

A variety shall be deemed to be essentially derived from another variety ("the initial variety") when

(i) it is predominantly derived from the initial variety, or from a variety that is itself predominantly derived from the initial variety, while retaining the expression of the essential characteristics that result from the genotype or combination of genotypes of the initial variety,.

This further requirement in indent (i) is inconsistent with indent (iii) (Kiewiet, 2002). To avoid this inconsistency, the Community Plant Variety Right Regulation 2100/94 of 27 July 1994[11], which is based on the UPOV 1991 Act, contains a definition of EDV that has not taken over the last part of Article 14 (5) (b) (i) UPOV 1991 Act.

6. For the purposes of paragraph 5 (a), a variety shall be deemed to be essentially derived from another variety, referred to hereinafter as 'the initial variety' when:

a) it is predominantly derived from the initial variety, or from a variety that is itself predominantly derived from the initial variety;
b) it is distinct in accordance with the provisions of Article 7 from the initial variety; and
c) except for the differences which result from the act of derivation, it conforms essentially to the initial variety in the expression of the characteristics that results from the genotype or combination of genotypes of the initial variety.

By doing so, the Community PVR system, one of the largest systems under the regime of UPOV, also has obviously put the focus on the genetic conformity between an EDV and its initial variety. This definition of EDV has also been incorporated in the PVR laws of Bulgaria, Czech Republic, Estonia, France, Germany, Romania and Slovenia[12].

Therefore, the focus of the discussion should be on indent (iii) of Article 14 (5) (b) of the UPOV 1991 Act. Indent (iii) stipulates that the EDV shall *conform to the initial variety in the expression of the essential characteristics that result from the genotype or combination of genotypes of the initial variety, except for the differences which result from the act of derivation*. Indent (iii) does not set a limit to the number of phenotypic differences between an EDV and the initial variety to one or a few [this is explicitly pointed out in the UPOV (1989) Doc. IOM/6/2, page 4, No. 12]. According to indent (iii) a variety shall be considered an EDV as long as its differences with the initial variety result from the act of derivation.

As far as vegetatively reproduced ornamental and fruit varieties are concerned it can be taken for granted that all phenotypic differences between a mutant and its mother variety result from the act of derivation.

When dealing with the regulatory aspects of NBTs, the High Level Group of Scientific Advisors (2017) dealt with spontaneous mutation, induced mutagenesis and genome editing technologies. In summary, they conclude: "The spontaneous mutation rate is about 7 x 10^{-9} base substitutions, per site, per generation. This results in one base substitution per generation in a genome the size of *Arabidopsis thaliana* (Ossowski et al., 2010). This means that unintended effects can also accumulate in sexual crossing. Induced mutagenesis, depending on intensity and concentration of the mutagenic agent, can increase this mutation rate by a factor of approximately 500 (Jander et al., 2003; Till et al., 2007; Cooper et al., 2008). All mutations occurring in addition to the mutations conferring the desired trait can be considered 'off-target'. There is a high probability that the random mutations in some genes will also influence the expression of other genes. Typically, however, the selected plants with the desired traits will still contain a high number of undetected random mutations, in particular if they do not cause disadvantageous phenotypic traits (Acquaah, 2015; Popova et al., 2015). Consequently, the breeder must undertake time consuming downstream selection in order to identify the desired traits essentially on the basis of the phenotype. This selection process does not exclude the presence of unidentified mutations in the new variety. The use of the new techniques involving ODM (oligo-directed mutagenesis) and SDN (site-directed nucleases) implies a different strategy. In this case the number of mutations is greatly reduced by comparison with the above and is limited to one or a few predefined mutations and possibly some off-target mutations."

Nevertheless, in general a mutant will also and always retain several important characteristics of its mother variety, because it was the very reason for the developer of the mutant to benefit from these important characteristics of the mother variety – this was the very reason why he had chosen this mother variety, and not e.g. a free, older variety.

CONCLUSION

After all, first generation varieties resulting from New Breeding Techniques, are mutants and thus are solely derived from their Initial Variety. This can have a direct impact on vegetatively propagated plants like ornamentals and fruits as existing varieties immediately can be improved by NBT. Therefore, for these crops, direct NBT varieties should always be considered EDV. However, applying NBT in other cultivated crops breeding activities can result in more

[11] Published in all EC-languages under www.cpvo.eu.int.
[12] The English texts are published under www.upov.int.

genetically narrow varieties too. First, the EDV concept is valid for all crops already although the delineation in seed crops is less straightforward than in vegetatively propagated plants. The high genetic conformity, which is obvious for mutants in fruits and ornamentals, needs then to be defined, mostly by using conformity measures based on an agreed set of molecular markers (in future this might become DNA sequence homology). Agreements on thresholds for genetic conformity have been made between breeders of certain species already. At the moment it merely deals with recurrent backcrossing and not too much with mutation breeding or use of NBTs. However, it can be expected that e.g. targeted mutagenesis by CRISPR/Cas and a short recurrent backcrossing cycle might become a future strategy in rapid cycling varieties e.g. vegetable breeding. If there continues to be an imbalance between the breeder of the initial variety that has created a new beneficial "mix" of genetic diversity within a genotype and NBT breeders that add selected improvements on existing varieties, an erosion and narrowing of genetic diversity could be the result.

A too narrow interpretation of the EDV Concept, as currently applied by the Australian Government, deprives breeders of initial variety from effective protection and an additional income. It fails to meet the aim of the EDV Concept as implemented in the UPOV 1991 Act, but rather steps back to the scope of the UPOV 1978 Act.

AUTHOR CONTRIBUTIONS

EK described the legal aspects of EDV within the UPOV Acts and member state legislations. EDK contributed the technical explanations on NBT, and JDR coordinated the writing of the paper and reviewed it.

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REFERENCES

Acquaah, G. (2015). "Conventional Plant Breeding Principles and Techniques," in *Advances in Plant Breeding Strategies: Breeding, Biotechnology and Molecular Tools*, 115–158. doi: 10.1007/978-3-319-22521-0_5

CIOPORA. Position on Breeders' Exemption of April 2014 https://www.ciopora.org/ciopora-position-papers.

Cooper, J. L., Till, B. J., Laport, R. G., Darlow, M. C., Kleffner, J. M., Jamai, A., et al. (2008). Tilling to detect induced mutations in soybean. *BMC Plant Biol.* 8 (1), 9. doi: 10.1186/1471-2229-8-9

CPVO (2018). Annual report. https://cpvo.europa.eu.

Crespel, L., Pernet, A., Le Bris, M., Gudin, S., and Hibrand Saint Oyant, L. (2009). Application of ISSRs for cultivar identification and assessment of genetic relationships in rose. *Plant Breed.* 128 (5), 501–506.

EASAC. (2015). New breeding techniques. European Academies' Science Advisory Council For. Retrieved from http://www.easac.eu.eu.

European Commission (1985). 85/561/EEC: Commission Decision of 13 December 1985 relating to a proceeding under Article 85 of the EEC Treaty (IV/30.017 - Breeders' rights: roses). http://data.europa.eu/eli/dec/1985/561/oj.

Government of Australia (2002). Clarification of plant breeding issues under the Plant Breeder's Rights Act 1994. *Rep. Expert Panel Breed.*, 19–41. www.anbg.gov.au/breeders/essentially-derived-variety.html.

High Level Group of Scientific Advisors. (2017). New Techniques in Agricultural Biotechnology, Explanatory Note 02, https://ec.europa.eu/research/sam/pdf/topics/explanatory_note_new_techniques_agricultural_biotechnology.pdf, ISBN 978-92-79-66222-5, doi:10.2777/574498, KI-02-17-242-EN-N.

Hunter, R. B. (1999). Essentially Derived and Dependency, some examples, Intellectual Property Committee, CSTA, Vancouver BC, July 20, 1999.

International Seed Federation (2005). *Essential Derivation - Information and Guidance to Breeders* 1–10.

International Seed Federation (2012). View on IP.

Jander, G., Baerson, S. R., Hudak, J. A., Gonzalez, K. A., Gruys, K. J., and Last, R. L. (2003). Ethylmethanesulfonate saturation mutagenesis in Arabidopsis to determine frequency of herbicide resistance. *Plant Physiol.* 131 (1), 139–146. doi: 10.1104/pp.102.010397

Kiewiet, B. (2002). Plant Variety Rights in a Community context. Speech made at the occasion of a symposium organised by the "Vereniging voor Agrarisch Recht" on 11.9.2002, 1–6. https://www.genres.de/fileadmin/SITE_MASTER/content/Schriftenreihe/Band24_Gesamt.pdf.

Korzun, V., and Heckenberger, M. (2004). Methodik zur Bestimmung im wesentlich abgeleiteter Sorten (Identification of essentially derived varieties): 7–12. In *Analyse und Bewertung der genetischen Vielfalt in der Land-, Forst- und Fischereiwirtschaft zur Ableitung von Entscheidungskriterien für Erhaltungsmaßnahmen*. Tagungsband eines Symposiums am 27 September 2004 in Mareinsee, Neustadt a. Rbge.

Lange, P. (1993). Abgeleitete Pflanzensorten und Abhängigkeit nach dem revidierten UPOV-Übereinkommen. *GRUR Int.* 1993 (2), 137–143.

Leßmann, H. (2000). Weiterzüchtung und Sortenschutz - Entwicklung der gesetzlichen Regelung, Festschrift for Rudolf Lukes.

Ossowski, S., Schneeberger, K., Lucas-Lledó, J. I., Warthmann, N., Clark, R. M., Shaw, R. G., et al. (2010). The rate and molecular spectrum of spontaneous mutations in Arabidopsis thaliana. *Sci. (New York N.Y.)* 327 (5961), 92–94. doi: 10.1126/science.1180677

Popova, E., Mukund, S., Kim, H. H., and Saxena, P. K. (2015). "Advances in Plant Breeding Strategies: Breeding, Biotechnology and Molecular Tools," in *Advances in Plant Breeding Strategies: Breeding, Biotechnology and Molecular Tools*, 63–93. doi: 10.1007/978-3-319-22521-0

Till, B. J., Cooper, J., Tai, T. H., Colowit, P., Greene, E. A., Henikoff, S., et al. (2007). Discovery of chemically induced mutations in rice by TILLING. *BMC Plant Biol.* 7, 19. doi: 10.1186/1471-2229-7-19

UPOV (1989). International Union for the Protection of New Varieties of Plants. 4th meeting with International Organizations, Geneva, October 9 and 10, 1889, Revision of the Convention. *Reference document: relevant extract of document IOM/IV/2.* Available at https://www.upov.int/meetings/en/doc_details.jsp?meeting_id=17485&doc_id=167958.

UPOV Act (1991). International Union for the Protection of New Varieties of Plants, International Convention for the Protection of New Varieties of Plants, https://www.upov.int//upovlex/en/conventions/1991/content.html

UPOV (1992). International Union for the Protection of New Varieties of Plants, UPOV 6th Meeting with International Organizations - Essentially Derived Varieties, UPOV document 30 October 1992: 1–6, Annex 1–7.

UPOV (2017). International Union for the Protection of New Varieties of Plants, Explanatory Notes on EDV. https://www.upov.int/edocs/expndocs/en/upov_exn_edv.pdf.

UPOV (2019). International Union for the Protection of New Varieties of Plants, Explanatory Notes on EDV. https://www.upov.int/edocs/mdocs/upov/en/c_52/c_52_7_rev.pdf.

Van Der Kooij, P. A. C. E. (1997). Introduction to the EC Regulation on Plant Variety Protection, KLUWER LAW International, London – The Hague – Boston.

Vosman, B., Visser, D., Rouppe Van Der Voort, J., Smulders, M. J. M., and Van Eeuwijk, F. (2004). The establishment of "essential derivation" among rose varieties, using AFLP. *Theor. Appl. Genet.* 109 (8), 1719–1725.

Zhang, D., Besse, C., Cao, M. Q., and Gandelin, M. H. (2001). Evaluation of AFLPs for variety identification in modern rose. *Acta Hortic.* 546, 351–357.

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POLICY AND PRACTICE REVIEWS
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Biosafety Regulatory Reviews and Leeway to Operate: Case Studies From Sub-Sahara Africa

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While modern biotechnology and, specifically, genetic modification are subject of debate in many parts of the world, an increasing number of countries in Sub-Sahara Africa are making important strides towards authorizing general releases of genetically modified (GM) crop varieties for use by farmers and agribusinesses. Obviously, the documented economic and environmental benefits from planting GM crops—based on a track record of over two decades—are a major driver in the decision-making process. Another key factor is the increasing alignment of biosafety regulatory policies with progressive agricultural and rural development policies in Africa, resulting in—compared to past experiences—greater emphasis on anticipated benefits rather than risks in biosafety regulatory reviews. In several cases, this has led to expedited reviews of GM crop release applications, either for confined field trials or general environmental release, taking experiences and data from other countries into account. Such regulatory approaches hold promise as the pipeline of relevant, pro-poor GM crop applications is expanding as are the opportunities provided by novel plant breeding techniques. This review article analyses the shifting policy context in select African economies, resulting in adoption of new agricultural technology, and novel regulatory approaches used in biosafety decision-making. Case studies will be presented for Ghana, Kenya, Malawi, Nigeria and Uganda to analyze challenges, distill lessons learned and to present general policy recommendations for emerging economies.

Keywords: policy & institutional actions, biotechnology, biosafety analysis, regulation, genome editing

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CONTEXT AND METHODOLOGY: REGULATION–TECHNOLOGY INTERACTIONS

As is the case generally when new technologies are introduced in society, there have been strong claims about the benefits and perceived adverse effects of agricultural biotechnology, specifically regarding genetically modified (GM) crops, and more recently regarding emerging techniques in plant breeding such as genome editing. Early concerns regarding genetic modification stimulated,

from the 1980s onward, the creation of regulatory systems for food and feed safety and environmental risk assessment. In Africa, governments generally started the development of their national biosafety systems more recently and, as with other areas of safety regulation, the task has been difficult in terms of defining science-based regulations and enforcement. For most of them the Cartagena Protocol on Biosafety has set the starting point, as adopted in 2003 as a supplement to the Convention on Biological Diversity (CBD), and which seeks to address environmental impact from transboundary movement, management and safe use of genetically modified organisms (GMOs).

The adoption of regulatory policies for biosafety and food/feed safety should be seen as part of a broader emerging international regime increasingly affecting the access and use of genetic resources for food and agriculture. This international regime affects scientific leeway and freedom-to-operate in a major way: The development and deployment of new agricultural technologies gets increasingly regulated, and often impeded, as access to essential research inputs (such as genetic resources, or protected technology) and the release of research outputs such as new crop varieties, is slowed down or halted by overly restrictive regulations. This phenomenon is described in further detail in Komen (2012). Evidently, the existence of sovereign rights over a country's natural resources, including genetic resources, is now well established in international law. Traditionally, genetic resources for agriculture were considered a common heritage of humankind and generally there was free transnational flow and access to all biological materials wherever they were located. Over time this situation was perceived to cause asymmetry between countries with rich genetic resources, usually free providers of these resources, and countries without extensive biological resources but who used them in R&D and protecting research results as intellectual property. The CBD, from which the Cartagena Protocol on Biosafety originated, changed this concept and reinforced sovereign rights to States over their biological resources through "access and benefit sharing" (ABS) regimes. Rourke (2018) analyses the increasing legal obstacles to accessing genetic resources and concludes that:

> *"The culmination of these barriers renders some biological research untenable and can result in the abandonment of research projects before they even commence."* (Rourke, 2018)

The CBD's Cartagena Protocol on Biosafety, originally aimed at maximizing benefits of biotechnology for biodiversity conservation while minimizing adverse effects, tends to add to the complexity by emphasizing the "precautionary principle" in biosafety decision making, while providing only limited guidance on what constitutes a functional national regulatory framework. Therefore, it is the responsibility of national governments to come up with science-based and efficient biosafety policies. This is becoming critical as new agricultural technologies are emerging, such as those related to genome editing, for which new regulatory approaches and instruments may be required.

According to Wiener (2004), technology and regulation are generally regarded as adversaries, with regulation seen as inhibiting technological change. Particularly regarding GMOs, calls for precautionary regulation have been frequent and reflected in the Cartagena Protocol as well as in several national and sub-regional regulatory frameworks. In the same essay, Wiener (2004) emphasizes that technological change impacts regulation as well. For example, by introducing improved technologies and products, risk can be reduced leading to decreasing need for regulatory oversight. In addition, it is often argued that regulation may encourage innovation[1] and competitiveness by promoting the introduction of cleaner and more cost-effective technologies. In cases where the chosen regulatory instrument is appropriate and well designed, technological change will progress. A prerequisite, according to Wiener, is the presence of "policy entrepreneurs" or "policy innovators" who: *"[W]ill develop and test new forms and approaches to regulation for greater effectiveness, les cost, less caustic side effects, and other describable attributes."* Wiener's arguments are reaffirmed in OECD analyses on "regulatory reform", defined as "*changes that improve regulatory quality, that is, enhance the performance, cost-effectiveness, or legal quality of regulations and related government formalities."* (OECD, 1997).

While the present article does not aim at providing an academic analysis of biosafety regulation and regulatory reforms, it is important to point to emerging regulatory reforms, and factors driving those reforms, in several countries in sub-Sahara Africa. First and foremost, recent reforms reflect a growing body of literature regarding the actual benefits and adverse impacts of GM crops. Over time, as actual experience continues to grow in planting, processing and consuming GM crops, much clearer analyses emerge regarding their real impacts, which is in turn affecting regulatory approaches. For example, a recent study by the US National Academies of Science (NAS, 2016) undertook a thorough review of available primary literature. The study committee found little evidence to connect GM crops and their associated technologies with adverse agronomic or environmental problems. In addition, the committee also found that—while impacts differed greatly across different contexts—systematic reviews and formal meta-analyses of the performance of GM crops have consistently shown the following impacts:

- Reductions in yield damage by insects;
- Reductions in insecticide applications for target insect pests, resulting in substantial environmental and health benefits;
- Decreases in management time and increases in flexibility related to herbicide-resistant (HR) crops; and,
- Increases in gross (in some cases net) margins due to the adoption of GM crops, or combinations of all the above.

[1] Following World Bank (2011), this article uses a broad depiction of 'innovation', encompassing technological change and institutional change. Following World Bank's agricultural innovation systems sourcebook (2011), components of innovation include, in addition to a strong capacity in R&D, collective action and coordination, the exchange of knowledge among diverse actors, the skills, incentives and resources available to form partnerships and develop businesses, and enabling conditions that make it possible for actors to innovate.

(NAS, 2016)

More specifically, Qaim (2019) concludes that, based on an in-depth analysis of available literature: *"Over the last 20 years, a large number of studies have been conducted, analyzing the effects of GM crop adoption on yield, pesticide use, farm profits, and other outcomes in different parts of the world. A meta-analysis has evaluated these existing studies, finding that GM crop adoption benefits farmers in most situations (…). On average, GM technology has increased crop yields by 22% and reduced chemical pesticide use by 37% (…). GM seeds are usually more expensive than conventional seeds, but the additional seed costs are compensated through savings in chemical pest control and higher revenues from crop sales. Average profit gains for adopting farmers are 68%.* (Qaim, 2019)

Analysis such as published by NAS (2016) increasingly play a role in biosafety decision-making as regulators become better able to weigh risks against benefits. This article takes a country case-study approach to further explore this development, using experiences from select countries in Africa. We will investigate recent progress and lessons learned, drawing recommendations for future policy reforms.

EVOLVING POLICY CONTEXT FOR AGRICULTURAL BIOTECHNOLOGY IN SUB-SAHARA AFRICA

Recognizing the important (potential) benefits of biotechnology to improving food security and rural development, governments across Africa have taken steps to establish an enabling policy framework to support adoption of biotechnology including GM crops and derived products. A more detailed analysis of relevant policies and regulations is presented below. Examples of recent policy decisions regarding GM crops include:

- Approvals for general release and commercial variety registration for insect-resistant, GM cotton hybrids in Ethiopia (2018), Kenya (2019), Malawi (2019) and Nigeria (2018). While farmers in Ethiopia started planting GM cotton at limited scale in 2019, GM seed distribution in Kenya, Nigeria and Malawi will start in 2020;
- Approval for general release and submission for variety registration for insect-resistant, GM cowpea in Nigeria (2018). Next step in this process will involve the registration, by the National Variety Release Committee, of GM cowpea as a new commercial variety followed by seed distribution by local companies.

In addition, with countries such as Ghana, Kenya and Uganda moving steadily from confined field trials (CFTs) towards general release applications, the setting for GM crop production in sub-Sahara Africa is rapidly changing. Until recently, only South Africa, Sudan and Burkina Faso had approved commercial production of GM crops. Right now, the regulatory pipeline is expanding and diversifying as illustrated by **Table 1**.

This increasing emphasis on agricultural biotechnology as a critical element in agricultural development policies is an important factor driving the expanding GM crop pipeline in Africa. Illustrative examples of such policies are presented below.

Agricultural Policies Increasingly Supportive of Innovation

As noted in a recent analysis by AGRA, the Alliance for a Green Revolution in Africa (2018), agriculture is key to Africa's future considering that the continent has most of the world's arable land, over half of the African population is employed in the sector, and it is the largest contributor to total gross domestic product (GDP). Yet, Africa is still producing too little food and agricultural value-added products (AGRA, 2018). Productivity in the agricultural sector has been broadly stagnant since the 1980s. Similarly, government investments in agricultural R&D show a slightly declining trend. However, recent successes in achieving rapid agricultural growth (e.g., in Ethiopia) have encouraged governments to adopt much more growth-orientated policies, which are highlighted in this section.

Ghana's government in 2017 launched an ambitious initiative to industrialize Ghana with the establishment of agro-processing factories in each of the 216 districts in the country. This initiative dubbed "one-district-one-factory" is to be implemented through the private sector. The factories are expected to utilize raw materials readily available in the district where the factory is located. This program, coupled with another government initiative, "Planting for Food and Jobs", is expected to boost agricultural production. This initiative has as its core: *"[T]he drive to motivate farmers to adopt improved, certified seeds and fertilizers through a private-sector marketing framework, by raising incentives and complimentary service provisions on the usage of inputs, good agronomic practices, marketing of outputs."* (MOFA, 2017). While implementation of such programs may be slower than anticipated, together with supportive policies aimed at a more market-orientated agricultural sector, they provide clear guidance to technology developers testing and planning the release of GM crops in Ghana.

Kenya's "Vision 2030", an overarching development policy aimed at becoming a middle-income country, focuses on agriculture as a key sector, which should drive the economy to an annual growth rate of around 10%. Agricultural policy in Kenya prioritizes a sharp increase in productivity and income growth, especially for smallholder farmers. More recently, the country's President's "Big 4 Agenda" emphasizes food security as the number one priority. This includes, among other elements, enhancing availability of basic staples such as maize, rice and potatoes, supporting agro-processing enterprises and enhancing large-scale crop production including cotton as an industrial crop. This Agenda acted as a boost to accelerating the introduction of GM, insect-resistant cotton. Revival of cotton production and local processing is among the Big 4 Agenda priorities and includes the large-scale planting of GM cotton to boost productivity.

For the past few decades, Malawi, like many other countries has been a net importer of food. Considering the challenge to become more self-sufficient and the important role agriculture

TABLE 1 | Biotechnology crop pipeline in Ghana, Malawi, Nigeria and Uganda (active projects, 2019).

Product	Trait	Developer	Collaborating Institutes	Regulatory Status (year of approval)
		GHANA		
Rice	Nitrogen use efficiency/water use efficiency/salt tolerance	Arcadia Biosciences	CSIR[1]—Crops Research Institute	CFT[2] (2013)
Cowpea	*Maruca* podborer resistance	CSIRO[3], AATF[4]	CSIR—Savannah Agricultural Research Institute	CFT (2013)
		KENYA		
Maize	Drought tolerance	Bayer Crop Science	KALRO[5], AATF, CIMMYT[6]	Approved for NPT (2016)
	Drought tolerance, insect resistance	Bayer Crop Science	KALRO, AATF, CIMMYT	CFT (2012)
	Stacked event of insect resistance and drought tolerance	Bayer Crop Science	KALRO, AATF, CIMMYT	CFT (2015)
Cotton	Insect resistance	Mahyco	KALRO	NPT (2016)
Sorghum	Biofortified sorghum with enhanced Vit A, Iron and Zinc	Pioneer Hi-Bred	KALRO, Africa Harvest	CFT (2015)
Cassava	Virus resistance (cassava brown streak disease)	DDPSC[7]	KALRO	CFT (2013)
	Virus resistance (African Cassava Mosaic Virus (ACMV) and Cassava Brown Streak Virus	MMUST[8]		CFT (2014)
Sweet potato	siRNA to sweet potato virus disease resistance	DDPSC	KALRO	CFT (2014)
		MALAWI		
Cotton	Insect resistance	Mahyco	DARS[9]	Commercial varieties registered (2019)
Cowpea	*Maruca* pod borer resistance	CSIRO, AATF	LUANAR[10]	CFT (2015)
Banana	Bunchy top virus resistance	QUT[11]	DARS	CFT (2016)
Plantain	Bunchy top virus resistance	QUT	DARS	CFT (2018)
		NIGERIA		
Cassava	Virus resistance; improved nutritional quality	DDPSC	NRCRI[12]	CFT approved (2019)
	Improved shelflife	IITA[13]		CFT (2018)
Cotton	Insect resistance	Mahyco	IAR[14]	Commercial varieties registered (2018)
Cowpea	Maruca pod borer resistance	CSIRO, AATF	IAR	General release approved (2018); submitted for variety registration (2019)
Rice	Nitrogen use efficiency/water use efficiency/salt tolerance	Arcadia Biosciences, CIAT, AATF	NCRI[15]	CFT (2014)
Soybean	Herbicide tolerance	MSU[16]	NABDA, NCRI	CFT approved (2019)
		UGANDA		
Banana	Disease resistance	AATF, IITA	NARO[17]	Multi-location CFTs (2010)
	Nematode resistance		NARO	CFT (2012)
	Improved nutritional quality	QUT	NARO	CFT (2011)
Cassava	Virus resistance	DDPSC	NARO	Multi-location CFTs (2010)
Maize	Drought tolerance/insect resistance	Bayer Crop Science, AATF	NARO	Multi-location CFTs (2015)
Potato	Fungal resistance	CIP[18]	NARO	Multi-location CFTs (2015)
Rice	Nitrogen use efficiency/water use efficiency/salt tolerance	Arcadia Biosciences, CIAT, AATF	NARO	CFT (2012)
Soybean	Herbicide tolerance	MSU	NARO	Contained research (2016)

[1]*CSIR, Council for Scientific and Industrial Research.*
[2]*CFT, Confined Field Trial.*
[3]*CSIRO, Commonwealth Scientific and Industrial Research Organisation, Australia.*
[4]*AATF, African Agricultural Technology Foundation.*
[5]*KALRO, Kenya Agricultural and Livestock Research Organisation.*
[6]*CIMMYT, International Maize and Wheat Research Center.*
[7]*DDPSC, Donald Danforth Plant Science Center, USA.*
[8]*MMUST, Masinde Muliro University of Science and Technology.*
[9]*DARS, Department of Agricultural Research Services.*
[10]*LUANAR, Lilongwe University of Agriculture and Natural Resources.*
[11]*QUT, Queensland University of Technology, Australia.*
[12]*NRCRI, National Root Crops Research Institute.*
[13]*IITA, International Institute for Tropical Agriculture.*
[14]*IAR, Institute for Agricultural Research.*
[15]*NCRI, National Cereals Research Institute.*
[16]*MSU, Michigan State University.*
[17]*NARO, National Agricultural Research Organisation.*
[18]*CIP, International Potato Center.*

plays in national development, the government of Malawi defined a Growth and Development Strategy (MGDS) in order to enhance agricultural growth, alleviate poverty and improve quality of life (Government of Malawi, 2017). The MGDS-III is a medium-term strategy designed to contribute to the country's long-term development goals. The current strategy covers a period of five years, from 2017 to 2022, with the objective to move Malawi to a productive, competitive and resilient nation primarily through sustainable agriculture while addressing water, climate change, and environmental management and population challenges. In the implementation plan/operation matrix, under agriculture sector, the Strategy identifies commercial application of agricultural biotechnologies as one of the priority activities which can contribute to increased agricultural production and productivity. In line with the MGDS, Malawi has secured a loan from the World Bank to transform Malawi's agricultural productivity through irrigation for period of 2019 to 2022. The objective of the project is to pull people out of poverty raising income levels of beneficiaries by overcoming the main production challenges of droughts and pests. These government initiatives indicate strong positive political will, which is critical to the sound regulation and adoption of any technologies including GM crops.

Nigeria's Agriculture Promotion Policy (2016–2020) document, titled, *"The Green Alternative" aims to "build an agribusiness economy capable of delivering sustained prosperity by meeting domestic food security goals, generating exports, and supporting sustainable income and job growth"* (FMARD, 2016). As the policy emphasizes, among other priorities, the need for productivity enhancements and innovation in Nigerian agriculture, and securing private sector investments, it has encouraged recent decisions to authorize the commercial release of GM crops such as insect-protected cotton and cowpea.

Agricultural policies in Uganda have been supportive towards exploiting the potential of GM crops since the development of the Plan for Modernization of Agriculture (PMA), some 20 years ago. The current overarching policy instrument, the Agriculture Sector Strategic Plan (ASSP) recognizes the need to enhance sustainable agricultural productivity and value addition using well-coordinated technological and service interventions (MAAIF, 2015). This policy further identifies the need to develop and implement a specific policy and regulatory framework for biotechnology in agriculture. In addition, the National Agricultural Research Act, 2005 was formulated with a key objective of transforming agricultural production into a modern science-based market-oriented system that is efficient, sustainable and profitable. The National Biotechnology and Biosafety Policy (2008) further strengthens the Government's commitment to utilize modern biotechnology tools for national transformation. These policy statements continue to guide GM research at the National Agricultural Research Organisation (NARO) in priority commodities such as maize, banana, and potato in line with the country's overall development policy statement, the Vision 2040, that also articulates the various sectors where biotechnology is seen as a strategic tool. These include agriculture, healthcare, industrial development, and environmental management.

Functional Regulatory Frameworks Support Technological Change

In addition to the overall supportive policy initiatives sketched above, it is important to note that these countries have invested in establishing functional regulatory frameworks for GM crops, allowing decision makers to weigh potential benefits against potential adverse effects on the environment and human or animal health. A science-based and practical regulatory framework has become an important enabling factor for countries researching and adopting GM crops. **Table 2** provides an overview of regulatory frameworks for countries covered in this article.

In countries that are selected as case studies for this article, there has been progress in recent years in establishing functional national biosafety frameworks and growing expertise in GMO decision-making. An overview of key legal instruments and institutional setups is provided in **Table 2**. Generally, while it is very well possible to use existing legislation to regulate biotechnology and GMOs, countries have opted to develop new biosafety laws and centralized decision-making bodies – such as national biosafety authorities. This has proven to be an effective approach in most cases, while responding to the need for clear legal authority, as evidenced by the number and range of regulatory decisions made in recent years (presented in **Table 1**).

Clear legal authority through comprehensive biosafety laws has still provided regulatory agencies with options to adopt flexible and innovative approaches to GM decision making. This has, for example, included decisions to (i) accept field trial data from neighbouring countries to expedite reviews of applications for confined field trials (CFTs); (ii) accept data from local GM CFTs and multi-location trials to shorten procedures for variety registration trials; (iii) accept food/feed safety dossiers and assessments from trading partners for accelerated safety decision-making. The following examples serve to illustrate these points.

- In Ghana, the National Biosafety Committee (NBC) approved multi-locational trials (MLTs) for insect-resistant GM cotton in 2012 after accepting data from confined field trials (CFTs) conducted previously in Burkina Faso. Considering the similar agro-ecological zones for cotton production in the two countries, the National Biosafety Committee (NBC) decided to grant an exemption for local CFTs and move to MLTs right away. These trials were put on hold in 2016 due to Burkina Faso's decision to terminate the commercial registration of GM cotton.
- Nigeria adopted the same principle—accepting data from other countries—and authorized country-wide MLTs for GM cotton prior to endorsing its general release and commercial variety registration in 2018.
- Kenya adopted fast-tracked protocols for variety registration trials involving GM crops that have gone through CFTs and MLTs, shortening the time required for DUS/VCU[2] performance trials from two planting seasons to one.

[2] DUS/VCU, Distinctness, Uniformity and Stability/Value for Cultivation and Use.

TABLE 2 | Biosafety regulatory frameworks in Ghana, Kenya, Malawi, Nigeria and Uganda (2019).

Cartagena Protocol Status (year ratified)	National Biosafety Law (year passed)	National Competent Authority	Subsidiary Regulations, Guidelines (year adopted)	Scientific Advisory Body
		GHANA		
Ratified (2003)	Biosafety Act (2011)	National Biosafety Authority (NBA)	–Biosafety implementing regulations (2019) –General release guidelines (2016) –Guidelines for handling requests (2016)	Technical Advisory Committee (TAC)
		KENYA		
Ratified (2003)	Biosafety Act (2009)	National Biosafety Authority (NBA)	–Contained use regulations (2011) –Environmental release regulations (2011) –Import, export and transit regulations (2011) –Labeling regulations (2012)	Board of Directors
		MALAWI		
Ratified (2009)	Biosafety Act (2002)	Environmental Affairs Department (EAD)	Biosafety (Management of Genetically Modified Organisms) Regulations (2007)	National Biosafety Regulatory Committee (NBRC)
		NIGERIA		
Ratified (2003)	National Biosafety Management Agency Act (2015)	National Biosafety Management Agency (NBMA)	National Biosafety Regulations (2017)	–National Biosafety Committee (NBC) –National Biosafety Technical Committee (NBTC)
		UGANDA		
Ratified (2001)	Biosafety law pending Presidential assent; field trials regulated under Uganda National Council for Science and Technology Act (1990)	Uganda National Council for Science and Technology (UNCST)	–National Guidelines for Field Trials of Genetically Engineered Plants (2011) –National Guidelines for Containment (2007)	National Biosafety Committee (NBC)

These examples confirm that, increasingly, governments in Africa can adjust their regulatory decision-making processes based on accrued scientific evidence.

Political Challenges Remain

While the above sketched progress in regulatory decision-making is encouraging, it is important to note that, still, most African countries are only slowly progressing in implementing functional regulatory frameworks. And, even in countries where recent progress has been achieved, there is considerable potential for backsliding. Many governments experience political opposition to GM crops and modern agriculture generally, and proposed biosafety legislation and regulations are conveniently associated with "opening the gateways" for the introduction of GMOs. Political opposition is in most cases fuelled by anti-GM activism, which has slowed down or halted the adoption of biosafety legislation (see, for example, Afedraru, 2019). For a continent that could benefit greatly from improved planting material including GM crops, this progress is slow.

As analysed in detail by Komen and Koch (2017), despite significant effort and donor-agency resources devoted to biosafety capacity development, and despite progress in some countries such as those presented above, many countries still do not have adequate capacity to design and implement biosafety regulations. This remains a significant barrier to the testing and adoption of new crop varieties, including those developed by genome editing and other plant breeding innovations, which would open new opportunities to grow more food, enhance incomes and reduce environmental impact of agriculture. An uncertain regulatory environment discourages private and public sector investment into development of the pro-poor crops and traits that farmers need the most.

While many donor-funded support programmes have attempted to build national capacity for the regulation of GM crops, progress is uneven at best. An early analysis of this situation was presented by Johnston et al. (2008) and is still very relevant. Their report confirms that generally, countries with existing capacity for biotechnology R&D, that already receive applications for activities with GMOs, and that have high-level political support for biotechnology and biosafety capacity building, have made most advances and have benefited most from technical assistance (Johnston et al., 2008). This assessment found that a majority of developing countries, including most countries of Africa, Central Asia, Oceania and the Caribbean, were not yet able to manage modern biotechnology and implement their national biosafety

frameworks. This general situation was confirmed in an independent evaluation commissioned by the CBD Secretariat in 2012 (CBD, 2012), and only slow progress has been made since then – with notable exceptions as indicated in this article.

For countries making progress despite the general challenges sketched above, important obstacles often occur at advanced stages of the regulatory process, when general release applications and commercial variety registration decisions are considered. In such cases, again based on analysis from countries that are focus for this article, the following hurdles occurred:

1. Lack of inter-ministerial collaboration and harmonization: As GM crops approach general release or market authorizations, government agencies become involved with responsibility for, e.g., food/feed safety, variety registration or, in some cases, for Environmental Impact Assessment (EIA). This has led to delays, inconclusive "conditional" release decisions and sometimes standstills in cases where these agencies lack familiarity with the biosafety regulatory review processes and tend to repeat safety reviews that were already completed. Early investment in establishing a coordinated, multi-agency framework is essential, coupled with policy consultations regarding harmonization of legal mandates.
2. Post-release requirements: Towards the final stages of the regulatory review process, post-release requirements are being considered related to, among other things, product labeling, product liability, co-existence, monitoring and surveillance. These concepts are in many cases not yet implemented and tested in African countries, associated expertise is low, and enforcement will be problematic. In the early phases of regulatory framework definition in Africa, strict post-release requirements were usually formulated and only later it is realized that these will form an impractical impediment to technology deployment.
3. High-level political will wavers: Finally, in the final stages of the decision-making process, government authorities get hesitant to fully authorize commercial cultivation of a GM crop particularly when this involves a GM food crop. The expected political/electoral consequences of such decisions, including the potential for public controversy, often affect such decisions. It also affects the decision-making regarding required policy reforms, as seen in the cases of (i) the continuation of a *de facto* GMO import ban in Kenya (Mukonyo, 2019), and (ii) the refusal by the President of Uganda to assent to a biosafety act that was passed twice by the Parliament of Uganda (Afedraru, 2019).

These hurdles have resulted in the current emphasis on primarily conducting CFTs with only slow progress towards general release and commercial cultivation, except for a non-food crop such as GM cotton. With the recent decision in Nigeria to authorize general release of GM cowpea, and its imminent registration as a commercial variety, this situation might change in the near future.

PLANT SCIENCE MOVING AHEAD: APPLICATION OF GENOME EDITING FOR IMPROVEMENT OF STAPLE CROPS IN AFRICA—THE CASE OF BANANA AND CASSAVA

While the R&D pipeline in Africa and, worldwide, adoption of GM crops steadily grows—in 2018, a total of 192 million hectares were planted with GM crops in 26 countries (ISAAA, 2018)—the emerging "new breeding techniques" (NBTs) are the latest addition to the plant breeder's toolbox as they offer the possibility of making genetic changes more precisely by targeting them to specific sites in the genome[3]. Especially the new tools for genome editing, like ODM (oligonucleotide mutagenesis) or CRISPR/Cas9 provide mechanisms to not just randomly increase genetic variation, as done by radiation or chemical mutagenesis, but also to precisely introduce mutations in genes of known functions to either impair or improve their function. NBTs have the potential to reduce the cost and time of bringing new products to the market since, compared with conventional breeding techniques, they can reduce the number of unwanted traits that might be co-transferred during the breeding process and that subsequently need to be removed. The greatest potential advantages of NBTs are their relative ease, precision, speed, and low cost, allowing breeders to focus more on the local growing conditions and to react more quickly to the changing needs and wants of growers and consumers.

With specific reference to sub-Sahara Africa, this precise genome editing has potential to revolutionize crop improvement. Notably, CRISPR/Cas9 has emerged as a powerful genome editing tool that can be used efficiently to induce targeted mutations in the genomes of plants species to produce improved varieties. CRISPR/Cas9 technology has been successfully applied in many organisms, including several plant species (Scheben et al., 2017). It has not only been established for model plants like *Arabidopsis* and *Nicotiana banthemiana* but also for complex crops like rice, wheat, maize, sorghum, tomato, soybean, apple, citrus, poplar, coffee (Ricroch et al., 2017; Breitler et al., 2018).

As in previous episodes of rapid changes in agricultural technology, the international centers that are part of the Consultative Group for International Agricultural Research (CGIAR) are at the forefront of incorporating NBTs in their research portfolio, in collaboration with national research organizations in sub-Sahara Africa. As a case in point, the International Center for Improvement of Maize and Wheat (CIMMYT, its acronym in Spanish), the Kenya Agriculture and Livestock Research Organisation (KALRO) and Corteva (formerly, DuPont Pioneer) have joined hands to exploit the gene editing (CRISPR-Cas) technology to improve maize and wheat germplasm. A specific example where this technology will be employed is to address maize lethal necrosis (MLN), a

[3] It is beyond the scope of this article to provide a detailed introduction on NBTs. For an excellent introduction, refer to the series of factsheets published by the European Plant Science Organisation, EPSO (2016). URL: https://epsoweb.org/epso/fact-sheets-on-new-breeding-technologies/2016/03/21/

devastating viral disease that has spread rapidly in many countries of East Africa since it was first detected in Kenya. CIMMYT identified a strong source of resistance against MLN, have fine-mapped it to a 1 MB region of chromosome 6, and expect to isolate the gene that confers resistance. Among the first targets for gene editing will be the parents of long-standing commercial hybrids in East Africa that were developed before the appearance of MLN and have since become susceptible to the disease. The International Institute of Tropical Agriculture (IITA), one of the CGIAR is on the forefront of applying NBT for improvement of banana for developing resistance to diseases (Tripathi L. et al., 2019; Tripathi J.N. et al., 2019; Maxmen, 2019). Details are provided below.

While most of the CRISPR/Cas9 based genome editing is reported in seed crops, recently it is also reported in vegetatively propagated crops like banana, cassava and potato (Butler et al., 2016; Odipio et al., 2017; Kaur et al., 2017; Naim et al., 2018; Ntui et al., 2019). Genome editing provides enormous opportunities for improvement of economically important traits of, polyploid, heterozygous and vegetatively propagated crops such as banana and cassava. Illustrative examples are summarized below.

Banana and cassava are among the important staple food and income generating crops for resource-poor farmers in Africa. Their contributions in the African diet are comparable to wheat, rice, maize, or potatoes in other parts of the world. The banana and plantain grown in Africa, is a starchy staple and the major source of carbohydrates to millions of poor people. Similarly, cassava is the most important primary food staple in several African countries. However, there are important biotic and abiotic constraints shattering the production of these important crops in Africa. Therefore, improvement of banana and cassava for economically important traits is critical to fulfill the food demand.

Tackling Banana Diseases Through CRISPR

Recently, CRISPR-based genome editing of banana has been demonstrated through knocking out the marker gene phytoene desaturase (PDS) leading to albino phenotype, however, the achieved mutation efficiency of 59% was quite low for practical application (Kaur et al., 2017). Further, higher efficiency (100%) of genome editing was reported for dessert banana with using CRIPSR construct with polycistronic gRNAs targeting PDS gene (Naim et al., 2018). Similarly, high mutation efficiency was also reported by IITA using PDS gene as target (Ntui et al., 2019; Tripathi L. et al., 2019). Once the efficient protocol for CRISPR/Cas9-based genome editing was established, this technology was utilized to inactivate the endogenous Banana streak virus (eBSV) integrated in the host genome, overcoming a major challenge in banana breeding (Tripathi J.N. et al., 2019).

BSV is a prevalent virus pathogen developing disease symptoms as chlorotic streaks on leaves and advancement of disease leads to killing of the plant. BSV belong to pararetroviruses, integrated into the host genome and known as endogenous BSV (eBSV). The viral sequences of eBSV are integrated in the B genome derived from Musa balbisiana. Cultivated varieties of banana are polyploid (AA, BB, AAA, AAB, ABB) descended from wild progenitors *Musa accuminata* (A genome) or/and *Musa balbisiana* (B genome). Plantain (AAB), one of the economically important sub-groups of banana, contains one B genome. It is an important staple food crop in Africa. During BSV infection, multiple copies of eBSV sequences integrates at a single locus in the B genome of the host as direct, inverted and tandem repeats (Chabannes et al., 2013). These proviruses can be reactivated into the infectious episomal BSV under several environmental stress conditions. When the infected banana plants are stressed, a functional episomal BSV genome and infectious viral particles are created through recombination of integrated sequences of eBSV, leading to development of disease symptoms in plants. Micropropagation for multiplication of plants through tissue culture and conventional breeding may also trigger activation of eBSV. Hence, the main cause of major epidemics of BSV is not the natural transmission of virus through insect vectors or use of infected seed materials, but instead due to reactivation of integrated eBSV under unfavorable stress conditions. As a result, BSV has become one of the key constraints in genetic improvement of plantain through conventional breeding and also deployment of plantain hybrids.

The diploid progenitor *Musa balbisiana* (BB) or several genotypes with at least one B genome have tolerance to biotic and abiotic stresses and good agronomic traits, still cannot be used as parents in breeding programs. Tripathi J.N. et al. (2019) demonstrated that the endogenous eBSV can be inactivated through targeted knockout of viral sequences from the host plant genome through CRISPR/Cas9 based genome editing and reports a strategy for inactivation of even other endogenous viral genomes from the host plants. The genome-edited events of plantain 'Gonja Manjaya' with targeted mutations in the viral genome prevented proper transcription or/and translational into infectious viral proteins. The inactivation of eBSV into infectious viral particles was confirmed by testing the potted plants of these edited events under water stress conditions in the glasshouse. Seventy five percent of the tested plants remained asymptomatic under stress conditions, whereas all the non-edited control plants showed BSV disease symptoma. This is the first report of generation of genome-edited crop in Africa and lay the foundation for editing of banana for important traits such as disease resistance. The International Institute for Tropical Agriculture (IITA, Nigeria) is also developing banana varieties resistant to bacterial wilt and fusarium wilt diseases using CRISPR/Cas9 technology.

Improving Cassava Virus Resistance and Quality

Genome editing of cassava was established using the CRISPR/Cas9 technology for knocking out the Phytoene desaturase (MePDS) gene (Odipio et al., 2017). This technology was further utilized for developing cassava varieties with enhance resistance to the cassava brown streak disease (CBSD), caused by two species of Ipomovirus: Cassava brown streak virus (CBSV) and Ugandan cassava brown streak virus (UCBSV) (Gomez et al., 2018). CBSD is a major viral disease of cassava affecting

its production in Central and East Africa. Gomez et al. (2018) reported that targeted mutations in cassava translation initiation factor 4E (eIF4E) isoforms nCBP-1 and nCBP-2 reduces CBSD disease severity as demonstrated with low degree of disease symptoms and virus accumulation in storage tuberous roots upon glasshouse challenge of edited cassava lines with CBSV. Simultaneous mutations in the nCBP-1 and nCBP-2 genes conferred significantly higher resistance to CBSD, however complete resistance to CBSD was not obtained in this study. Therefore, authors recommended that improved varieties of cassava with complete resistance to CBSD can be developed by stacking this approach of disrupting eIF4E isoforms with other resistance strategy such as RNAi.

Further, researchers has attempted to apply this technology to develop enhance resistance to African cassava mosaic virus (ACMV), a geminivirus (Mehta et al., 2019). However, the effective resistance to ACMV was not achieved in the glasshouse challenge experiments. The authors linked this to the evolution of editing-resistant geminiviruses in edited cassava.

CRISPR/Cas9-based genome editing can be coupled to genetic improvements in cassava for traits such as starch improvement and early flowering. Bull et al. (2018) reported genome-editing of cassava for manipulating starch biosynthesis and improving the starch quality in the storage roots. They generated the edited cassava with mutations in two genes [PROTEIN TARGETING TO STARCH (PTST1) or GRANULE BOUND STARCH SYNTHASE (GBSS)] involved in amylose biosynthesis, leading to reduction or elimination of amylose content and finally improving the quality of in starch in cassava roots. The authors also demonstrated accelerated breeding by transferring Arabidopsis FLOWERING LOCUS T gene in the genome-editing events of cassava for early flowering. They further demonstrated edited cassava with modified starch can be segregated in greenhouse to produce transgene-free progeny with improved trait.

In order to meet the increasing demand of food with limited or same resources, better and effective ways to produce food are required. As summarized above, one option is to utilize new breeding tools like genome editing for crop improvement. Currently, severe endeavors are underway to enhance yields of banana and cassava—among a range of other crops—through generating improved varieties with resistance/tolerance to biotic stresses.

A major question to be addressed, from a regulatory perspective, will the products of NBTs be classified under the current definitions of genetic modification, or not? Over the last three decades, a patchwork of (draft) biosafety laws and regulations has emerged affecting the development and release of improved crops and resulting in trade issues when approvals are "asynchronous"[4]. In recent years, given the rapid advances in genome editing, there is increased regulatory attention and debate around these applications. Salient developments are outlined below; it should be emphasized that while an increasing number of regulatory authorities have provided clarity regarding their approach to genome edited crops, the jury is still out in major economic blocs such as the European Union.

[4]Asynchronous approval refers to the situation in which there is a delay in the moment when a GM event is allowed to be used in one country in comparison to another country. A notable case in point illustrating the trade disruptions from asynchronous GMO approvals concern the use of GM plant varieties that are approved in countries which export them to the EU, mainly in the form of animal feed (maize, soybeans), before these are actually approved by the EU.

EMERGING REGULATORY APPROACHES TO GENOME EDITING, WITH REFERENCE TO AFRICA

Considering the above sketched situation, where differences in GMO regulation are exacerbated by specific challenges posed by NBTs, different countries are responding in different ways to the question of how applications of NBTs should be classified, as regulated GM material or not. The key point here is that specific applications, e.g., when genome editing is used to create a loss of function of a target gene, result in an event that contains no "foreign DNA", i.e., no novel combination of genetic material and therefore cannot be distinguished from a product of conventional mutagenesis (which is commonly exempt from GM regulation).

Summary of Global Developments

As early as 2013, the European Academies Science Advisory Council (EASAC), a body of national science academies of the EU Member States, argued that products of NBTs should not fall under GMO legislation when they do not contain "foreign DNA". The EASAC advisors noted that in some cases the product cannot be distinguished from one generated by conventional techniques, and also argued that the new techniques allow much more precise and targeted changes compared with mutagenesis used in conventional breeding, where changes in the genome are induced by chemicals or radiation, creating multiple, unknown, and unintended mutations (EASAC, 2013).

Regulatory authorities in a range of countries follow this same EASAC conclusion that genome editing, in cases where no novel combinations of genetic material have been created, should be no more regulated than a product of conventional mutagenesis. An often-cited case in point is Argentina, where in 2015 a new regulation was issued aimed at clarifying the regulatory status of products from NBTs. The regulation allows applicants to consult with the competent authority early-on in the R&D stage ("design stage") to determine if a product developed using gene editing is a GMO or not. The prime decision-making factor here is if the product has a *novel combination of genetic material* or not. Preliminary consultations are then followed by a final determination based on a full information package describing the gene editing procedure and resulting changes in the genomic sequences of the end product (Lema, 2019). So far, this approach has resulted in regulatory exemptions for several genome edited crops in Argentina. Importantly, South American countries such as Brazil, Chile, Colombia and Paraguay have followed Argentina's lead and will regulate genome edited products on a

case-by-case basis and allow exemptions from GM regulation when there is no novel combination of genetic material. Similar approaches can be cited from major economies such as the USA, Japan and Australia. Such decisions regarding NBTs generally followed a thorough review of scientific evidence and existing regulations so that these remain fit for purpose in times of rapid technological development.

By contrast, in a major agricultural trading bloc like the EU there is still uncertainty as to how products from NBTs will be regulated. While EU bodies recognized the potential of NBTs early on, as evidenced by a range of studies and projects conducted with EU support, to date there has been no clear-cut policy decision or statement from the European Commission. So far its actions were limited to, among other things, requesting advisory notes from the EU Scientific Advisory Mechanism (SAM) and awaiting a legal opinion from the EU Court of Justice (CJEU). This wait-and-see approach has greatly complicated matters.

On 25 July 2018, the CJEU advised that organisms obtained by new mutagenesis techniques are considered as GMOs, within the meaning of the EU's Directive 2001/18/EC on the release of GMOs into the environment (the "GMO Directive"), and that they are subject to the obligations laid down by the GMO Directive (Curia Press and Information, 2018). Thus, the ruling considers genome edited organisms as GMOs, which do not fall under the existing exemption under the Directive for organisms resulting from conventional mutagenesis. The ruling adopts a strict legal interpretation of what constitutes a GMO and does not consider the principle of "novel combination of genetic material" as applied in other jurisdictions – as summarized above. It should be noted that the Court ignored this principle while the GMO Directive includes, in its definition of a GMO, the phrase *"has been altered in a way that does not occur naturally by mating and or natural recombination"*. This misunderstanding implies that organisms that have been edited but that can or do occur naturally, will have to follow the same European regulatory procedures as GMOs, including a detailed analysis of possible risks.

The Court ruling has been widely debated since its publication, which will not be summarized here. A clear analysis of its implications was issued by the European Commission's Group of Scientific Advisors (2018). The Group concludes that:

> *"[…] meeting the obligations of the GMO Directive implies cost- and labour-intensive pre-market evaluations and a long duration of the approval process, which are difficult and onerous to bear, particularly by small and medium enterprises. This may diminish incentives for investment, negatively affect research and innovation in this field, and limit the commercialisation of gene edited products."* (EC-SAM, 2018)

In particular, it is noted that:

> *"It is a concern that countries in the developing world exporting feed and food to the EU might not benefit from gene edited crops if they follow the EU authorisation practices, as some of them currently do. No single breeding technique alone can provide a magic bullet for solving the problem of unsustainable food production and food scarcity in the world. However, gene- editing has the potential to contribute to food security, which is particularly relevant given the growing world population and climate change."* (EC-SAM, 2018)

A critical challenge, also emphasized by EC-SAM (2018), to the EU decision-making process will be the fact that enforcement of obligations imposed by the GMO Directive, on traceability and labeling of GMOs entering the EU will be near-impossible. Due to the absence of a novel combination of genetic material, seeds and commodities developed with NBTs are identical to those developed through unregulated plant breeding or naturally occurring variations. As a result, the detection, identification and quantification of genome edited products will be a major challenge. This fact will become more problematic when exporting countries authorize the cultivation of genome edited crops that will not be regulated as GMOs.

In order to address this situation, EC-SAM recommends amending the EU's GMO Directive to reflect the growing track record of safe use and consumption and associated scientific evidence, in particular on genome editing and established techniques of genetic modification, considering the obligation for GMO legislation to be: *"[C]lear, evidence-based, implementable, proportionate and flexible enough to cope with future advances in science and technology in this area"* (EC-SAM, 2018).

Emerging Regulatory Approaches in Sub-Sahara Africa

Considering the situation sketched above, and the important influence the EU has in shaping regulatory policies in Africa due to trade relations and historical ties, it is encouraging to note that sub-Sahara African governments have started defining their own regulatory approaches to GMOs and, increasingly, applications of NBTs. Based on growing expertise worldwide and in-country with safety reviews and decision-making on GMOs, including general releases of GM insect-resistant cotton and cowpea, regulatory authorities are now getting ready for NBTs and genome editing. Apart from global regulatory developments in other parts of the world, there are several important drivers behind regulatory policy formulation in Africa, including:

1. Rapid technological developments resulting in the first contained-use applications involving NBTs being recently submitted to regulatory authorities in Africa, for example, in Kenya by international research centers.
2. Discussions as part of the CBD's bi-annual inter-governmental meetings regarding synthetic biology, gene drives, genome editing, among other items, which often take a highly precautionary view on emerging technologies generally and NBTs in particular, including the calling for moratoriums (Callaway, 2016), which were refuted by a majority of African delegates.

3. Policy consultations under the umbrella of the African Union, proposing more enabling and science-based approaches to emerging technologies such as gene drives and genome editing. While the Union's work on genome editing started only recently, its report on gene drives clearly embraces the technology as a realistic option for effective disease control (AU-NEPAD, 2018).

Spurred by these developments, a few governments are considering the inclusion of NBTs and other emerging technologies in their regulatory frameworks. A case in point is Nigeria, where, in August 2019, an amended biosafety act for Nigeria was published in the government gazette following assent by the country's President. The amendments broaden the scope of the act to wider "biosecurity" concerns, not just biosafety, and to include applications of genome editing, gene drives and synthetic biology as regulated technologies along with GMOs. At this stage, no specific assessment criteria and procedures were defined, nor criteria for possible exemptions. This approach may be effective as it brings the new tools and technologies under the purview of a functional regulatory agency; however, it may open the door for regulating genome editing innovations as if they are GMOs. Further work will be undertaken by Nigeria's National Biosafety Management Agency (NBMA), which would lead to a science-based guideline that would help implement the amended Act by including clear regulatory triggers for genome edited organisms.

Rather than amending its biosafety act, in Kenya the National Biosafety Authority (NBA) opted to develop a guideline on genome editing. Guideline development was deemed to be a suitable approach as it allows for flexibility, in a rapidly evolving field, and consultations with scientists and regulatory agencies in the agricultural and environmental sectors. Following initial consultations, NBA organized a technical meeting in April 2019 analyzing advances in genome editing, and relevant regulations in Kenya as well as other countries. Currently, the authority is drafting a guideline that aspires to be practical and science-based, and which allows for case-by-case reviews and exemptions from biosafety review for products that do not have a novel genetic combination. Thus, the proposed approach for Kenya essentially follows those adopted in Argentina and other South American countries.

It is expected that other countries that embrace agricultural biotechnology will soon follow Nigeria's and Kenya's lead and devise policy and regulatory approaches to NBTs and other emerging technologies.

WAY FORWARD AND RECOMMENDATIONS

In this article, we have pointed to several important recent developments in sub-Sahara Africa regarding the regulation and adoption of GM crops, as well as the continuing political challenges that hamper further progress. Regulatory authorities in select case study countries have gone through a period of rapid capacity development, as shown by the increasing number and scope of GMO environmental releases including CFTs and general releases and have shown flexibility in their decision-making processes. A major driving factor in this process constitute the more progressive agricultural and development policies as formulated by national governments. Recent capacity development will provide a foundation for the formulation and implementation of science-based regulations for novel breeding techniques such as genome editing.

While recent progress is encouraging, we fully acknowledge the fact that political challenges remain. A critical challenge involves the need to sustain the political will and current momentum that provides scientists with leeway to operate. While not discussed extensively in this article, it is generally recognized that controversies exist around the adoption of GM crops and that, despite a safety track record of over two decades, public opinion on this topic remains divided. These controversies are sometimes reflected in government decisions in sub-Sahara Africa, when decision-makers call for moratoriums on CFTs or bans on GM commodity imports. Such calls are influenced by activist groups who campaign against modern agricultural technologies generally, and against GMOs in particular. Recently, these campaigns have also resulted in court cases challenging biosafety decisions by national competent authorities. Despite this, progress in Africa continues but it involves a careful balancing act.

Governments and development partners will have to continue investing in the development of knowledge, skills and capacities required to regulate and adopt GM crops; and, in due course, the products emanating from genome editing applications—as introduced in this article. Emerging best practices from, e.g., Argentina, provide critical guidance. Capacity development should include outreach and awareness initiatives to ensure public debates and policy consultations are well informed and incorporating the best available science.

A special case is made here for enhanced regional and sub-regional collaboration. Increasingly, regulatory authorities in Africa are exchanging expertise and data regarding biosafety decisions, including the acceptance of data generated in neighboring countries. This collaboration would provide the basis for harmonization efforts in regional economic communities such as the Common Market for East and Southern Africa (COMESA), the Economic Community of West African States (ECOWAS) and the Southern African Development Community (SADC). Each of these regional bodies have initiated processes and guideline development towards sub-regional harmonization in the recent past but none have been adopted and implemented so far. A constructive development at the regional level involves the recent policy statements by the African Union (AU) regarding genome editing and gene drives for human health purposes, which have impacted discussions in AU member states. Such supportive statements will continue to be important to bolster the current momentum.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article/supplementary material.

AUTHOR CONTRIBUTIONS

All authors listed have made substantial, direct, and intellectual contribution to the work and approved it for publication.

REFERENCES

Afedraru, L. (2019). Uganda's anti-GMO activists blamed for stonewalling nation's new biosafety rules (Kampala, Uganda: Genetic Literacy Project). 6 May 2019. https://geneticliteracyproject.org/2019/05/06/ugandas-anti-gmo-activists-blamed-for-stonewalling-nations-new-biosafety-rules/.

AGRA (2018). Africa agriculture status report: catalyzing government capacity to drive agricultural transformation (Issue 6) (Nairobi, Kenya: Alliance for a Green Revolution in Africa).

AU-NEPAD (2018). Gene drives for malaria control and elimination in Africa. report from the high-level African panel on emerging technologies (Addis Ababa, Ethiopia: African Union - New Partnership for Africa's Development).

Breitler, J. C., Dechamp, E., Campa, C., Rodrigues, L. A. Z., Guyot, R., Marraccini, P., et al. (2018). CRISPR/Cas9-mediated efficient targeted mutagenesis has the potential to accelerate the domestication of Coffea canephora. *Plant Cell Tissue Organ Cult.* 134, 383–394. doi: 10.1007/s11240-018-1429-2

Bull, S. E., Seung, D., Chanez, C., Mehta, D., Kuon, J.-E., Truernit, E., et al. (2018). Accelerated ex situ breeding of GBSS- and PTST1-edited cassava for modified starch. *Sci. Adv.* 4, eaat6086. doi: 10.1126/sciadv.aat6086

Butler, N. M., Baltes, N. J., Voytas, D. F., and Douches, D. S. (2016). Geminivirus-mediated genome editing in potato (Solanum tuberosum L.) using sequence-specific nucleases. *Front. Plant Sci.* 7, 1045. doi: 10.3389/fpls.2016.01045

Callaway, E. (2016). Gene drive moratorium shot down at UN meeting. *Nat. Biotechnol.* 21 December 2016. doi: 10.1038/nature.2016.21216

CBD (2012). "Independent evaluation of the action plan for building capacities for the effective implementation of the cartagena protocol on biosafety," in Draft (Un-edited) Evaluation Report, requested by Secretariat of the Convention on Biological Diversity and United National Environment Programme (Montreal, Canada: Secretariat of the Convention on Biological Diversity).

Chabannes, M., Baurens, F. C., Duroy, P. O., Bocs, S., Vernerey, M. S., Rodier-Goud, M., et al. (2013). Three infectious viral species lying in wait in the banana genome. *J. Virol.* 87, 8624–8637. doi: 10.1128/JVI.00899-13

Curia Press and Information (2018). "Organisms obtained by mutagenesis are GMOs and are, in principle, subject to the obligations laid down by the GMO Directive. Court of Justice of the European Union, Press Release No. 111/18," in Judgment in Case C-528/16 Confédération paysanne and Others v Premier minister and Ministre de l'Agriculture, de l"Agroalimentaire et de la Forêt (Luxembourg: Curia Press and Information).

EASAC (2013). Planting the future: opportunities and challenges for using crop genetic improvement technologies for sustainable agriculture. EASAC policy report 21 (Halle, Germany: European Academies Science Advisory Council).

EC-SAM (2018). Statement by the group of chief scientific advisors: a scientific perspective on the regulatory status of products derived from gene editing and the implications for the GMO directive (Brussels, Belgium: European Commission, Scientific Advisory Mechanism).

EPSO (2016). Crop genetic improvement techniques factsheets. EPSO working group on agricultural technologies (Brussels, Belgium: European Plant Science Organization). https://epsoweb.org/epso/fact-sheets-on-new-breeding-technologies/2016/03/21/.

FMARD. (2016). Agriculture promotion policy 2016-2020: the green alternative (Abuja, Nigeria: Federal Ministry for Agriculture and Rural Development).

Gomez, M. A., Lin, Z. D., Moll, T., Chauhan, R. D., Hayden, L., Renninger, K., et al. (2018). Simultaneous CRISPR/Cas9-mediated editing of cassava eIF4E isoforms nCBP-1and nCBP-2 reduces cassava brown streak disease symptom severity and incidence. *Plant Biotechnol. J.* 17, 421–434. doi: 10.1111/pbi.12987

Government of Malawi (2017). *The malawi growth and development strategy (MGDS) III (2017 – 2022): Building a Productive, Competitive and Resilient Nation* (Lilongwe, Malawi: Government of Malawi). URL: https://www.mw.undp.org/content/malawi/en/home/library/the-malawi-growth-and-development-strategy-iii-.html.

ISAAA. (2018). Global status of commercialized biotech/GM Crops: 2018. Brief 54 (Ithaca, N.Y: International Service for the Acquisition of Agri-biotech Applications).

Johnston, S., Monagle, C., Green, J., and Mackenzie, R. (2008). Internationally funded training in biotechnology and biosafety: is it bridging the biotech divide? (Yokohama: UNU Institute of Advanced Studies).

Kaur, N., Alok, A., Shivani, Kaur, N., Pandey, P., Awasthi, P., et al. (2017). CRISPR/Cas9-mediated efficient editing in phytoene desaturase (PDS) demonstrates precise manipulation in banana cv. Rasthali genome. *Funct. Integr. Genomics* 18, 89–99. doi: 10.1007/s10142-017-0577-5

Komen, J., and Koch, M. (2017). "Building human capacity and skills in biosafety: lessons learned and emerging best practices. chapter 7," in *Genetically Modified Organisms in Developing Countries: Risk Analysis and Governance*. Eds. A. Ademola, E. Adenle, J. Morris and D. J. Murphy (Cambridge, U.K.: Cambridge University Press).

Komen, J. (2012). The emerging international regulatory framework for biotechnology. *GM Crops Food: Biotechnol. In Agric. Food Chain* 3:1, 78–84. doi: 10.4161/gmcr.19363

Lema, M. A. (2019). Regulatory aspects of gene editing in Argentina. *Transgenic Res.* 28, 147–150. doi: 10.1007/s11248-019-00145-2

MAAIF (2015). *Agriculture Sector Strategic Plan (ASSP)* (Kampala, Uganda: Ministry of Agriculture, Animal Industry and Fisheries). URL: https://www.agriculture.go.ug/agriculture-sector-strategic-plan-assp/.

Maxmen, A. (2019). CRISPR might be the banana's only hope against a deadly fungus. *Nat. News.* 574, 15. doi: 10.1038/d41586-019-02770-7

Mehta, D., Sťrchler, A., Anjanappa, R. B., Zaidi, S. S. A., Hirsch-Hoffmann, M., Gruissem, W., et al. (2019). Linking CRISPR-Cas9 interference in cassava to the evolution of editing-resistant geminiviruses. *Genome Biol.* 20, 80. doi: 10.1186/s13059-019-1678-3

MOFA. (2017). Planting for food and jobs: strategic plan for implementation (2017-2020) (Accra, Ghana: Ministry of Food and Agriculture). URL: https://www.mofa.gov.gh/site/business/pfj#.

Mukonyo, R. (2019). Will Kenya lift its GMO ban as its agriculture falters? *Alliance Sci.* October 10, 2019. https://allianceforscience.cornell.edu/blog/2019/10/will-kenya-lift-gmo-ban-agriculture-falters/.

Naim, F., Dugdale, B., Kleidon, J., Brinin, A., Shand, K., Waterhouse, P., et al. (2018). Gene editing the phytoene desaturase alles of Cavendish banana using CRISPR/Cas9. *Transgenic Res.* 27, 451–460. doi: 10.1007/s11248-018-0083-0

NAS (National Academies of Sciences, Engineering, and Medicine) (2016). Genetically engineered crops: experiences and prospects (Washington, DC: The National Academies Press).

Ntui, V. O., Tripathi, J. N., and Tripathi, L. (2019). Robust CRISPR/Cas9 mediated genome editing tool for banana and plantain (Musa spp.). *Curr. Plant Biol.* in press. doi: 10.1016/j.cpb.2019.100128

Odipio, J., Alicai, T., Ingelbrecht, I., Nusinow, D. A., Bart, R., and Taylor, N. J. (2017). Efficient CRISPR/Cas9 genome editing of Phytoene desaturase in cassava. *Front. Plant Sci.* 8, 1780. doi: 10.3389/fpls.2017.01780

OECD (1997). The OECD report on regulatory reform: synthesis (Paris, France: Organisation for Economic Co-operation and Development).

Qaim, M. (2019). "Genetically modified crops," in *Encyclopedia of Food Security and Sustainability*, vol. 3. Eds. P. Ferranti, E. M. Berry and J. R. Anderson (Amsterdam: Elsevier), pp. 159–164.

Ricroch, A., Clairand, P., and Harwood, W. (2017). Use of CRISPR systems in plant genome editing: toward new opportunities in agriculture. *Emerg. Top. Life Sci.* 1, 169–182. doi: 10.1042/etls20170085

Rourke, M. F. (2018). Access and benefit-sharing in practice: non-commercial research scientists face legal obstacles to accessing genetic resources. *J. Sci. Policy Gov.* 13(1). (October 2018). URL: http://www.sciencepolicyjournal.org/uploads/5/4/3/4/5434385/rourke.pdf.

Scheben, A., Wolter, F., Batley, J., Puchta, H., and Edwards, D. (2017). Towards CRISPR/Cas crops – bringing together genomics and genome editing. *New Phytol.* 216, 682–698. doi: 10.1111/nph.14702

Tripathi, L., Ntui, V. O., and Tripathi, J. N. (2019). Application of genetic engineering and genome editing for developing climate smart bananas. *Food Energy Secur.* 8, 4. doi: 10.1002/fes3.168

Tripathi, J. N., Ntui, V. O., Ron, M., Muiruri, S. K., Britt, A., and Tripathi, L. (2019). CRISPR/Cas9 editing of endogenous banana streak virus in the B genome of Musa spp. overcomes a major challenge in banana breeding. *Commun. Biol.* 2, 46. doi: 10.1038/s42003-019-0288-7

Wiener, J. B. (2004). The regulation of technology, and the technology of regulation. *Technol. Soc.* 26 (2004), 483–500. doi: 10.1016/j.techsoc.2004.01.033

World Bank. (2011). Agricultural innovation systems: an investment sourcebook (Washington, D.C: the international bank for reconstruction and development/The World Bank).

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Improving Risk Assessment in the European Food Safety Authority: Lessons From the European Medicines Agency

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The recent Regulation (EU) 2019/1381, published on the 6th September 2019, aims to improve the transparency and sustainability of the EU risk assessment in the food chain by amending the General Food Law Regulation (EC 178/2002) and a number of other regulations related to the food sector. This Regulation is introduced as a response to the Fitness Check of the General Food Law Regulation as well as a response to public concerns expressed by a European Citizens' Initiative on glyphosate and pesticides. This article evaluates the amendments introduced by Regulation 2019/1381with respect to the institutional and regulatory environment in the food chain and more specifically concerning the risk assessment procedure. For this purpose, we perform a comparison of the institutional and organizational characteristics of the European Food Safety Authority (EFSA) and European Medicines Agency (EMA) in relation to the processes of risk assessment and risk evaluation, especially the processes surrounding genetically modified foods and pesticides, and how these characteristics affect the politicization of these processes. We conclude that the risk assessment process followed by EFSA would have benefitted and become more effective and less politicized, if the recent Regulation 2019/1381 had introduced some of EMA's institutional structures and methods on risk evaluation.

Keywords: risk, assessment, food, regulatory, governance

INTRODUCTION

In the past, food policy was within the competence of the Member States in the European Union (EU). Following a series of crises in the late 1990s [the Bovine Spongiform Encephalitis (BSE) crisis, *E. coli* etc.], the Member States transferred the food policy competences, particularly with respect to food safety, to the EU institutions in the early 2000s. This transfer resulted in institutional and legislative changes and introduced a number of Regulations, Directives and

decisions. The Prodi Commission (1999–2003) created the Directorate General SANTE[1] and the General Food Law (GFL, Regulation 178/2002) established the European Food Safety Authority (EFSA) (Chatzopoulou, 2019b). These developments reflected the need for an integrated policy at the supranational level that could lead to harmonization of food and feed safety rules and marked the Europeanization of food policy across the EU Member States (Alemanno, 2006; Chatzopoulou, 2015, 2019a). European people received this food policy transition mostly positively (Eurobarometer[2], 2019, p. 28). However, EFSA has been criticized for lack of effectiveness particularly with respect to risk analysis, selection of data and information, risk communication; lack of transparency and broad representation of the available scientific knowledge (Chatzopoulou, 2015); and the long duration risk assessment processes[3], which also created delays in the subsequent authorization of applications (EuropaBio, 2016; Wesseler and Kalaitzandonakes, 2019). These concerns about transparency resulted in some degree of public dissatisfaction and contestation of EFSA's work. Moreover, concerns about conflict of interest among EFSA's experts led the European Parliament to withhold EFSA's budget resulting in stricter administrative rules (Chatzopoulou, 2015).

Following the adoption of the European Citizens' Initiative (ECI) Regulation in 2010[4], but before it entered into force, Greenpeace claimed to have collected 1 million signatures calling for a moratorium on genetically modified (GM) crops. During 2014–2018, the Commission launched the Fitness Check of the GFL Regulation, which also identified various concerns regarding the risk assessment of GM organisms (GMOs) and the governance of EFSA. In addition, following a series of critiques by various non-governmental organizations, an ECI, that had collected 1,070,865 signatories[5], to "Ban Glyphosate and Protect People and the Environment from Toxic Pesticides"[6] was presented to the Commission on the 23rd of October 2017. This initiative raised concerns on the transparency and sustainability of EFSA's risk assessment processes in the food chain. A public hearing was organized at the Parliament on 20 November 2017[7]. Responding to these concerns, the European Commission (EC) submitted on 11 April 2018 a regulation proposal to the Council and the European Parliament (EP) that led to Regulation 2019/1381. This Regulation introduced amendments in Regulation (EC 178/2002) on general food law and a number of Regulations related to GM food and feed (1829/2003) and feed additives (1831/2003) along with eight legislative acts dealing with specific sectors[8] in the food chain[9]. Thus, the paper focuses mainly on the regulated products GM and pesticides and not on non-regulated ones (e.g., contaminants). The amendments aim to improve the transparency, reliability and independence of studies submitted to EFSA in order to support EFSA's risk assessment process.

The Regulation emphasizes the proactive and automatic communication to the public, at an early stage of the risk assessment, of all studies submitted to EFSA for risk assessments via EFSA's website thereby strengthening the transparency and underpinning EFSA's assessments while protecting legitimate confidential business information[10]. Moreover, the Regulation introduces a greater involvement of the Member States in the Management Board in line with the inter-institutional "Common Approach on EU decentralized agencies[11]," as it is in the case of the European Medicines Agency (EMA). For instance, the Member States are encouraged to be active in the nomination of scientific panel experts for risk assessment. Such a change is expected to broaden the number and type of experts with respect to disciplines and geographical distribution.

Taking stock on the existing literature on risk governance, this paper addresses the overall question: *to what extent will the recent Regulation, on the transparency and sustainability of the EU risk assessment in the food chain, improve the risk assessment process in EFSA and increase trust among the European people?*

To address this question, this paper links the amendments made by the Regulation, in the governance of risk analysis for EFSA, to the corresponding ones in EMA. This comparison is relevant in understanding the governance of risk assessment because EFSA and EMA belong to the same cluster of agencies, both are under DG SANTE and their areas of expertize are connected, both agencies consider aspects of health and environment and perform risk assessment for products that will be introduced to the market[12]. The foundation of both agencies, aimed to ensure that risk assessment processes, are based on objective scientific knowledge. However, the governance of risk assessment of food and feed biotechnology in EFSA has been highly contested, in comparison to medical biotechnology in EMA. This contestation is also accompanied by a low acceptance of food and feed biotechnology. For example, the acceptance of genetic modification by society differs among the two sectors, e.g., food and agriculture and health and medicine (Olynk Widmar et al., 2017).

The paper is structured as follows: After presenting the competences and governance structures of EFSA and EMA, the

[1]Initially known as SANCO.

[2]https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/Eurobarometer2019_Food-safety-in-the-EU_Full-report.pdf, Special Eurobarometer Wave EB91.3.

[3]https://chemicalwatch.com/15504/efsa-delays-bpa-exposure-assessment https://www.icis.com/explore/resources/news/2008/12/10/9178492/basf-slams-efsa-delay-on-amflora-safety-decision/.

[4]http://www.europarl.europa.eu/factsheets/en/sheet/149/european-citizens-initiative.

[5]http://ec.europa.eu/citizens-initiative/public/initiatives/successful.

[6]http://ec.europa.eu/transparency/regdoc/rep/3/2017/EN/C-2017-8414-F1-EN-ANNEX-1-PART-1.PDF. The initiative was registered 25/01/2017 and was answered 12/12/2017.

[7]http://ec.europa.eu/transparency/regdoc/rep/3/2017/EN/C-2017-8414-F1-EN-MAIN-PART-1.PDF.

[8]These are GMOs, smoke flavorings, food contact materials, food additives, food enzymes and flavorings, plant protection products and novel foods.

[9]http://www.europarl.europa.eu/legislative-train/theme-environment-public-health-and-food-safety/file-transparency-and-sustainability-of-the-eu-risk-assessment-in-the-food-chain.

[10]http://europa.eu/rapid/press-release_MEMO-18-2942_en.htm.

[11]https://ec.europa.eu/food/sites/food/files/gfl_transparency_comm_proposal_synopsis_20180410_en.pdf.

[12]We did not compare EFSA to EEA or ECDC, for example, because these two agencies do not perform risk assessment of products for the market. We did not chose EEA and ECHA because they do not directly provide scientific opinions to DG SANTE as both EFSA and EMA do.

following section discusses the real problem that raises criticisms, over time, in relation to the governance of risk assessment in EFSA. A description of the policy process is also presented, followed by the discussion of the results.

THE MAIN CRITICAL ISSUE: BACKDROPS OF RISK MANAGEMENT PROCESS

The founding of EFSA and EMA aimed to support the Commission's work by providing scientific based opinions based on risk assessment and risk evaluation processes respectively. However, EFSA's risk assessment opinions on food and feed biotechnology have been criticized, especially with respect to transparency (publication of studies used for the assessment[13]) and demonstrated politicization elements (Löfstedt, 2004; Chatzopoulou, 2015). EMA, on the other side, does not face such critiques concerning biomedicine and genetic medicine. This article suggests that this difference is related to the dissimilar governance of risk assessment in these two agencies, implicating directly the risk management processes. One contrasting difference is the role of the member states in the risk assessment process. The member states' involvement matters as it shapes, as it would be expected, the governments' attitudes and possibly also the public opinion. Regulatory systems and *ad hoc* decisions are not only a response to public attitudes but they also contribute to forming public attitudes in a significant way (Qaim, 2016, p. 117).

Olynk Widmar et al. (2017) demonstrate that GM acceptance in the society differs among sectors, e.g., it depends on if GM food and feed are used and associated with human health or with plant biotechnology. These studies show that GMOs used in pharmaceutical production do not face the same contestation as GMOs used directly for food or food processing (Qaim, 2016). For example, a series of scientific controversies among member states created delays during the risk management processes in the case of maize[14] (Qaim, 2016; Eriksson and Chatzopoulou, 2017). Following the risk assessment process by EFSA, the disagreements emerge in the comitology that consists of civil servants from all Member States and oversees the Commission's use of delegated powers. When qualified majority voting (QMV) cannot be reached in this committee, then the Appeal Committee can overrule the Commission by QMV. Most often, the Appeal Committee ends up with no decisions and then the Commission has the final responsibility[15] (Christiansen, 2019, p. 111). In the great majority of cases, this results in (1) a favorable scientific opinion by EFSA, (2) no opinion through comitology, or (3) threats of court cases of inaction (ibid). In the case of medicines registration by EMA, there is no comitology procedure. Formally, the Commission's decision is based on EFSA's risk assessment opinion. And although the Commission has authorized GMO applications in the past years for food and feed use, these decisions were not for cultivation. *If the decision would have only been based on EFSA's risk assessment*, several additional GM products for food and feed, or also for cultivation *might* have been approved by the EC. Consequently, it can be argued that in practice there is still a moratorium on the approval of GMOs for cultivation, as the only GM crop that has been authorized for cultivation in recent years (the Amflora potato) had its authorization annulled in 2013. The EU Court argued that there was a procedural error in the approval process (General Court of the European Union, 2013) due to insufficient involvement of the Member States in the standing committee by the Commission. In other words, the final rejection of the Amflora potato was based on national politics and interests and not on EFSA's science based risk assessment. Although the EU introduced an opt-out mechanism (Directive EU 2015/412) in 2015 which allowed member states to restrict or prohibit cultivation of authorized GM crops in their territory, this did not resolve these issues (Eriksson et al., 2019).

Such incidents reflect a broader uncertainty with respect to the risk management at the Commission level (following EFSA's risk assessment), which the existing decision-making and governance processes have not been able to address adequately. These incidents also demonstrate the importance of the national views and interests in the decision-making, which seem not to be based on EFSA's scientific risk assessment on safety for health and the environment (Qaim, 2016, p. 116). Thus, politicization is leading to outcomes that are not based on scientific knowledge, affecting the legitimacy and reputation of the governance of risk assessment processes and the role of EU institutions, namely EFSA.

In light of these arguments, this paper analyses to what extent the current development with the Regulation 2019/1381 will be able to address effectively issues on the governance of EU risk management. For this purpose, we compare the institutional and organizational characteristics of EFSA and EMA with respect to the risk assessment process, which constitutes the basis of risk management by the Commission. This comparison is expected to allow us to unfold and understand the necessary changes in the EU institutional and regulatory environment with respect to risk assessment and the risk management procedure on food biotechnology. Such changes can potentially contribute to elimination of delays and promote innovation in food biotechnology in a responsible manner.

THE INSTITUTIONAL STRUCTURES AND RISK ASSESSMENT IN EFSA AND EMA

Despite their similarities, the two agencies, EFSA and EMA, follow different governance structures, which affect their functioning, reputation, and legitimacy. Governance provisions and structures determine the control mechanisms used by the agencies' principals (the Commission and the Member States). EFSA is the most recently founded of the two agencies, and as above mentioned, it was established in 2002. Furthermore, while the risk evaluation of medicines has been harmonized

[13]https://www.foodnavigator.com/Article/2019/04/17/Europe-s-new-rules-for-food-safety-approval-Building-trust-in-science.

[14]http://www.arc2020.eu/pioneers-gm-maize-1507-a-case-history/.

[15]Please see Eriksson et al. (2019) and Lehrman (2014) for a detailed presentation of the authorization process in the comitology procedure.

BOX 1 | The three interconnected components of risk analysis according to the EU General Food Law, Regulation 178/2002 (L31/7, L31/8).

9. "Risk" means a function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard;
10. "Risk analysis" means a process consisting of three interconnected components: risk assessment, risk management and risk communication;
11. "Risk assessment" means a scientifically based process consisting of four steps: hazard identification, hazard characterization, exposure assessment and risk characterization;
The risk assessment must be undertaken in an independent, objective and transparent manner based on the best available science.
12. "Risk management" means the process, distinct from risk assessment, of weighing policy alternatives in consultation with interested parties, considering risk assessment and other legitimate factors, and, if need be, selecting appropriate prevention and control options; (Regulation 178/2002:7.
13. "Risk communication" means the interactive exchange of information and opinions throughout the risk analysis process as regards hazards and risks, risk-related factors and risk perceptions, among risk assessors, risk managers, consumers, feed and food businesses, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions;' (Regulation 178/2002:8).

more at the global level, in the case of certain food aspects, such as GMOs, there is significant divergence concerning risk assessment processes (e.g., process versus product based)[16]. EFSA's establishment aimed to provide independent scientific advice and clear communication on existing and emerging risks in the area of food and feed safety, animal health and welfare as well as plant health (European Food Safety Authority, 2014).

The GFL (Regulation 178/2002)[17] defined the rules for the entry of new food and/or feed products into the EU market, established EFSA, and set out certain procedures related to food safety. The GFL provides four measures: (1) the establishment of the Rapid Alert System for Food and Feed (RASFF), (2) the Standing Committee on Plants, Animals, Food and Feed (PAFF), (3) the adoption of emergency measures, and (4) the establishment of a general plan for crisis management. In addition, it includes three inter-related components of risk analysis: risk assessment, risk management and risk communication (**Box 1**).

The GFL also defined the principles of EFSA governance. Taking into account the opinion of the EP, the Commission proposes EFSA's 14-member Management Board. The selection is based on the members' experience and expertize and not on nationality (European Food Safety Authority, 2011), but it should secure the broadest possible geographic distribution within the Union (Reg. 178/2002, Art. 25). This process constituted an innovation in the EU agencies' governance, since until then territorial representation in the agencies Management Board was important. Additionally, four of the Management Board members should represent organizations such as consumers and other interests in the food chain (European Food Safety Authority, 2011).

The Management Board appoints an Executive Director who is responsible for the implementation of the financial rules of the Authority and has to ensure the adequate organization of the legality of transactions (European Court of Auditors, 2011). The Executive Director also has the responsibility for the day-to-day management of EFSA and is supported by the Heads of department, Heads of unit, the Chief Scientist and the Senior Policy Adviser[18]. A Scientific Committee and 10 Scientific Panels (corresponding to different policy areas[19]) and their working groups supports EFSA's risk assessment work. According to the existing legislation, the Scientific Committee[20] and the scientific panels provide the Authority's scientific opinions to the Commission, each within their own spheres of competence (Commission Regulation (EU), 2017). The Scientific Committee consists of the chairs of the Scientific Panels complemented by six independent scientific experts who do not belong to any of the Scientific Panels and focuses on the coordination and consistency of the scientific opinion procedure (Reg. 178/2002). The scientific panels are composed of independent scientific experts who carry out scientific assessments, organize public hearings where necessary, and develop related assessment methodologies. These are appointed for 3-year periods, similar to the ones in EMA. However, they do not secure the geographic representation of all member states as it occurs in EMA's scientific committees.

When EFSA receives a market application first validates its completeness or if it needs more information to proceed. Then EFSA's relevant Panel establishes a working group that develops a draft and submits it to the Panel for discussion and often to public consultations. For example, for the GMO Panel, there are three permanent working groups: molecular data, food and feed, and environmental risks). The working group consists of members of the relevant Panel and a number of additional scientists from specialist fields. This working group assesses the available scientific information from the Member States, research institutes or companies. EFSA may request more data directly from the applicant. An important aspect is the defining of a timetable of the process from the beginning, which depends on each case. The adoption of the assessment, usually a scientific opinion (it can also be a Statement, Guidance Document or another type of output), is based on majority in the relevant Panel at a plenary meeting[21].

Based on EFSA's risk assessment, the Standing Committee on Plants, Animals, Food and Feed (PAFF)[22] under the Commission decides the final authorization of the product.

[16]Point suggested by one of the reviewers.

[17]https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32002R0178&from=EN.

[18]http://www.efsa.europa.eu/en/people/operationalmanagement.

[19]Panel on Animal Health and Welfare (AHAW), Panel on Biological Hazards (BIOHAZ), Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), Panel on Contaminants in the Food Chain (CONTAM), Panel on Food Additives and Flavorings (FAF, Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Panel on Genetically Modified Organisms (GMO), Panel on Nutrition, Novel Foods and Food Allergens (NDA), Panel on Plant Health (PLH) and PPR.

[20]The latest mandate for the Scientific Committee and the ten panels began on 1 July 2018.

[21]http://www.efsa.europa.eu/en/howwework/workingpractices.

[22]https://ec.europa.eu/food/committees/paff_en.

The PAFF is an intergovernmental committee composed of representatives of all Member States and is chaired by a European Commission representative that also exemplifies the networked characterization of the EU agencification[23]. Its mandate covers the entire food supply chain – from animal health issues on the farm to the product on the consumer's table. The PAFF plays a key role ensuring that the EU measures on food and feed safety, animal health and welfare, and plant health are practical and effective. The PAFF delivers opinions on draft measures that the Commission, who is responsible for the risk management, intends to adopt. This is the first committee where all the member states are represented in the risk analysis process. But, this Committee constitutes part of the risk management not the risk assessment (scientific level) and constitutes a significant difference when compared to EMA.

Similarly to EFSA, EMA consists of scientific committees, seven of them, and a number of working parties and related groups, which conduct the scientific work. The EU pharmaceutical legislation was introduced in 1965 as a reaction to the thalidomide scandal (malformation effects on babies by the medicine for pregnant women). EMA was founded in 1993 by merging the pre-existing Committee for Human Medicinal Products (CHMP) former CPMP (Committee for Proprietary Medicinal Products) and the Committee for Veterinary Medicinal Products (CVMP). This merger initially created the European Agency for the Evaluation of Medicinal Products (EMEA) that was renamed as European Medicines Agency (EMA) in 2004[24]. EMA's was expected to further the efficient and flexible implementation of EU legislation on pharmaceuticals, and ensure rapid access of new products to the Community market (Sauer, 1996, p. 23, as cited Groenleer, 2009, p. 145). In order for a medicinal product to be placed on the EU market, it has to follow the core pharmaceutical regulation, namely the marketing authorization requirement. There are three different procedures for authorizing medicines: the centralized procedure, the mutual recognition/decentralized procedure and the national procedure (Wirtz, 2017). For certain biotechnology-derived and high tech products the centralized procedure is mandatory. While the marketing authorization is granted by the EU Commission, the scientific assessment of the application is carried out by the EMA.

Each of the EMA committees follows its own rules of procedure. Each committee appoints a rapporteur who prepares an assessment report, which the committee will consider and eventually adopt as part of a scientific opinion or recommendation. For certain procedures, a "co-rapporteur" also prepares an assessment independently from the rapporteur[25]. The work of the rapporteur and co-rapporteur is supported with resources and expertize by an assessment team with necessary expertize and resources. In addition, the EMA secretariat provides technical, scientific and administrative support for each assessment. In order to mobilize the best expertize for medicines evaluation, regardless of where experts are geographically based, rapporteurs and co-rapporteurs can establish multinational assessment teams by including experts from other Member States as well as their own. The EMA committees try to reach their conclusions by consensus whenever possible, but if not the committee holds a vote, which follows specific procedures and rules[26]. For this purpose, Member States have to liaise with the Management Board and the EC in order to ensure that the final composition of the Committees covers the scientific areas relevant to its tasks. The committee considers the final assessment report and eventually adopts it as part of a scientific opinion or recommendation.

Since 2004, CHMP carries out the assessment and evaluation. This Committee often consults the Pharmacovigilance Risk Assessment Committee (PRAC) in relation to risk assessment. Directive 2001/83/EC and Regulation (EC) No 726/2004 lay down specific rules concerning the pharmacovigilance of medicinal products for human use and set up the PRAC. Accordingly, the PRAC is responsible for the risk management of the use of medicinal products for human use including detection, assessment, minimization and communication related to the risk of adverse reactions, design and evaluation of post-authorization safety studies and pharmacovigilance audit.

Both the CHMO and PRAC committees consist of a Chair and one member and one alternate member appointed by each of the EU Member States and one member and one alternate member appointed by each of the EEA-EFTA States. The EC also appoints several representatives. Two experts (one member and an alternate) on clinical pharmacology and pharmaco-epidemiology to ensure that the relevant expertize is available within PRAC, other two (one member and one alternate), to represent healthcare professionals; and finally two more (one member and one alternate) to represent patient organizations. All members, except those appointed by EU and EEA-EFTA states, are appointed based on a public call for expressions of interest and after consulting the EP based on their relevant expertize in pharmacovigilance matters and risk assessment of medicinal products for human use. The members and the alternates of the Committees are appointed for a term of 3 years, which may be prolonged once. The aim is to guarantee the highest levels of specialist qualifications and a broad spectrum of relevant expertize. Since all Member States are involved in the risk evaluation as part of the scientific committees for pharmaceuticals, scientific differences in national opinions are resolved before the EMA provides its scientific opinion to the Commission, who then mostly rubberstamps EMA's opinions.

When concerns over the safety or benefit-risk balance of a medicine or class of medicines are raised, a referral procedure, which can be started by the EC, a Member State or the company that markets the medicine, is used to resolve such

[23]For a detailed description of the process (see Lehrman et al., 2014, p. 69–70), https://www.slu.se/globalassets/ew/org/centrb/mbiot/publikationer/shapingourfood_mistrabiotech_web_140625.pdf.

[24]REGULATION (EC) No 726/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 31 March 2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Text with EEA relevance) (OJ L 136, 30.4.2004, p. 1).

[25]https://www.ema.europa.eu/en/committees/how-committees-work.

[26]https://www.ema.europa.eu/en/committees/how-committees-work; https://www.ema.europa.eu/documents/other/prac-rules-procedure_en.pdf.

issues. In a referral, the medicine, or class of medicines, is "referred" to EMA so that it can conduct a scientific assessment on behalf of the EU and then make a recommendation for harmonized position across the EU. There are a number of reasons why a referral may be started, ranging from concerns over the safety to disagreements among Member States on the use of the medicine. Safety-related referrals are assessed by the PRAC and then either by the CHMP or, for nationally authorized medicines, by the Coordination Group for Mutual Recognition and Decentralized Procedures-Human (CMDh). All other referrals on human medicines are assessed by the CHMP only. For most referrals, the EC issues a decision to all Member States reflecting the measures to take to implement the Agency's recommendation[27].

CHRONOLOGY OF EVENTS

Figure 1 presents a chronological record of events since the GFL founding in 2002 until the submission of the legislative proposal by the Commission to the EP and the Council in April 2018. In December 2010, Greenpeace and Avaaz submitted a pilot ECI with one million signatures in accordance with the rules established by the Lisbon Treaty in 2009. This first pilot ECI responded to the first authorization in 12 years by the Commission in March 2010, for the cultivation of a GM crop in Europe[28]. The 2010 ECI called for a moratorium on all new authorizations and a review of the GM approval process, claiming that the existing authorization raised serious health and environmental concerns. As the ECI process was not formally implemented at this point, the EU institutions did not have to take action. Years later, in March 2015, in disagreement with EFSA's scientific opinion, the International Association for Research Cancer (WHO, IARC) "classified glyphosate as 'probably carcinogenic to humans' (Group 2A)," which triggered a lot of concern about the objectivity of science in the society. Between 23/10/2017 until 17/01/2018, a most recent ECI "Ban glyphosate and protect people and the environment from toxic pesticides" was launched, which indicated concerns on the transparency in the risk management process by EFSA. This recent ECI became one of the four successful ECIs since the Regulation (EU) No 211/2011 Article 11(4) of the Treaty of the European Union was put into practice in 2012[29] and the Commission responded according to the Lisbon Treaty rules.

Furthermore, during 2014–2018, the Commission launched a Fitness Check in order to address if the existing GFL is still "fit for purpose" regarding its relevance and effectiveness, efficiency, coherence, and whether it should be simplified so that it can become less costly. The Fitness Check recognized the positive outcomes of the EU food and feed safety policy, but it also acknowledged that there is space for improvement in "the implementation of the functional separation of the risk assessment and risk management at EU level, set out in the GFL Regulation"[30]. In addition, the Commission received feedback 20/12/2017-17/01/2018 and started an Open Consultation 23/1/2018-20/3/2018. Moreover, this was discussed at various fora with different actors, namely the Advisory Group on the Food Chain and Animal and Plant Health[31]; the EFSA Advisory Forum (national food safety authorities on 6th February 2018); the Commission Expert Group on General Food Law[32] (5th March, 2018) and finally the Scientific Committee of EFSA[33] (14 and 15/02/2018). This demonstrates a long process that involved a variety of public and private actors, before the Commission formulated its legislative proposal on 11/04/2018.

CHANGES INTRODUCED BY THE RECENT COMMISSION REGULATION 2019/1381 ON THE TRANSPARENCY AND SUSTAINABILITY OF THE EU RISK ASSESSMENT IN THE FOOD CHAIN

On 11 April 2018, the Commission submitted a proposal to the Council and the Parliament for a regulation on the transparency and sustainability of the EU risk assessment in the food chain. This proposal regulation aimed to amend the GFL Regulation (EC 178/2002) and a number of other regulations related to, amongst others, GM crop cultivation, food and feed uses (1829/2003), and food and feed additives (1831/2003). The recent Reg. 2019/1381 addresses aspects of governance and by introducing a change in the composition of the Management Board, in a way, recognizing the importance of the representation of all member states, as it is the case in EMA:

"It is thus appropriate to include representatives of all Member States of the European Parliament and of the Commission as well as of civil society and industry organizations in the Management Board, while providing that those representatives should have experience and expertize not only in the fields of food chain law and policy, including risk assessment, but also in the fields of managerial, administrative, financial and legal matters and ensuring that they act independently in the public interest" (Reg. 2019/1381, Art.14, L231/3).

[27] https://www.ema.europa.eu/human-regulatory/post-authorisation/referral-procedures.

[28] http://www.greenpeace.org/eu-unit/en/News/2010/first-citizens-initiative/.

[29] http://europa.eu/rapid/press-release_IP-18-2563_en.htm.

[30] https://ec.europa.eu/food/sites/food/files/gfl_fitc_executive_summary_2018_en.pdf.

[31] The Advisory Group on Animal and Plant Health discussed the Commission's proposal on transparency and sustainability of the EU food and feed safety risk assessment model on 5 February 2018.

[32] REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the transparency and sustainability of the EU risk assessment in the food chain amending Regulation (EC) No 178/2002 (on general food law), Directive 2001/18/EC (on the deliberate release into the environment of GMOs), Regulation (EC) No 1829/2003 (on GM food and feed), Regulation (EC) No 1831/2003 (on feed additives), Regulation (EC) No 2065/2003 (on smoke flavorings), Regulation (EC) No 1935/2004 (on food contact materials), Regulation (EC) No 1331/2008 (on the common authorization procedure for food additives, food enzymes and food flavorings), Regulation (EC) No 1107/2009 ([on plant protection products) and Regulation (EU) No 2015/2283 (on novel foods) https://ec.europa.eu/transparency/regdoc/rep/1/2018/EN/COM-2018-179-F1-EN-MAIN-PART-1.PDF.

[33] Fifteen trade and business associations, four Non-Governmental Organizations (NGOs), one Member State (MS), and one citizen submitted feedback. 471 people participated in the OPC, 318 citizens and 153 stakeholders.

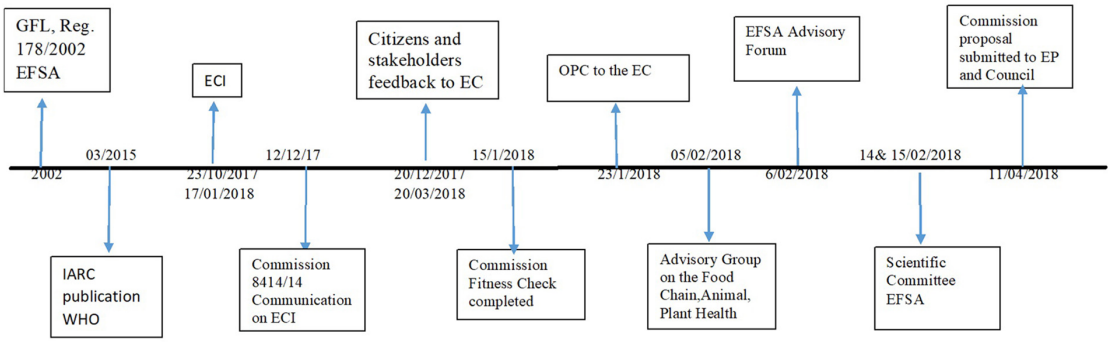

FIGURE 1 | Timeline of events in relation to the Commission's legislative proposal for GFL until the EC submitted its proposal to EP and Counsil.

Responding to the shortcomings in the Authority's high level expertize identified by the Fitness Check (Art. 16, L231/3), the new Regulation emphasizes the importance of greater involvement of the Member States in the Management Board by nominating scientific panel experts for risk assessment. This change would be more in line with the inter-institutional Common Approach on Union Decentralized Agencies in the effort to increase the consistency of the EU agencies' management board model. Such a change is expected to broaden the number and type of experts with respect to disciplines, number, and geographical distribution. In order to do so, it is suggested to provide better financial compensation, which is currently considered low, in order to attract highly qualified experts. However, expansion of the Management Board (Reg. 2019/1381) and the number of candidates does not adequately address the problems in the actual structure of the risk assessment process, which is directly linked to the expertize of the Authority's scientific panels. Neither, "a more active role to ensure that a sufficient pool of experts is available to meet the needs of the Union risk assessment system" of the Management Board or the member states in the appointment of the scientific panels' members would be sufficient (Reg. 2019/1381). This change does not describe precisely what is an "active role" and how this could ensure "high level of scientific expertize, independence and multidisciplinary expertize." While the national scientific organizations are involved "in drafting preparatory scientific opinions to be peer-reviewed and adopted" (Art. 18) by the scientific panels they are not represented in the preparation phase (ibid).

Regulation 2019/1381 focuses significantly on risk communication through: (1) Automatic publication of all studies and supporting information submitted to EFSA for risk assessment, in an electronic format that would be publicly available and easily accessible; (2) Stakeholders would be consulted on submitted studies, and confidentiality would be protected in justified circumstances; (3) A specific procedure would be implemented for renewals of substances already authorized; and (4) The Commission would, via delegated act, adopt a general plan for risk communications in the agrifood chain (Comitology Newsletter #52, 2018). While this is important, it raises concerns in the industry concerning confidentiality and property rights with implications on research and innovation in the sector[34]. Most importantly, these changes do not tackle the identified concerns on the risk assessment process adequately as they concentrate on the risk communication.

When the EP received the proposal from the Commission, the Special Committee on the EU authorization procedure for pesticides (PEST) was established and held 12 meetings during 2018. In the EP the Environment, Public Health and Food Safety Committee (ENVI) has been assigned the responsibility to write the report. The first Rapporteur was Renate Sommer (EPP, DE), who suggested in its draft report that the EP would prefer to align the EFSA rules with those of other EU agencies (e.g., the EMA) as much as possible, but ensure that confidential information does not become available at the time the application is submitted but when EFSA adopts its final opinion[35]. Early publication of information could jeopardize innovation and jobs creation as the industry would be reluctant to invest in EU countries. Renate Sommer resigned[36] in protest at the final shape of her report, when the plenary voted by 427 in favor (172 against, 67 abstentions) of amendments[37] to the draft EFSA reform on 11 December 2018. Mrs Sommer characterized the decision a "populist" move that will harm innovation and "endanger the whole food chain." The Spanish MEP Pilar Ayuso González took over the representation in trilogues, despite her vote against the final EP report. The Council reached an internal position in December.

During the process, there were many disagreements in the Council. For example, the Dutch government criticized several elements, in particular the notion of granting EFSA more funds to fulfill the required extra tasks. **Figure 2** presents a

[34]https://www.bechbruun.com/en/news/2019/new-eu-food-regulation-may-influence-the-disclosing-of-legitimate-business-information.

[35]https://www.europarl.europa.eu/doceo/document/A-8-2018-0417-AM-132-140_EN.pdf?redirect.

[36]https://www.euractiv.com/section/agriculture-food/news/new-food-transparency-rules-risk-falling-victim-to-eu-institution-spat/ and https://www.euractiv.com/section/agriculture-food/news/meps-ready-to-negotiate-efsas-transparency-rule-but-need-to-find-a-new-negotiator/.

[37]The EP suggested 112 amendments (see amendments at http://www.europarl.europa.eu/doceo/document/A-8-2018-0417_EN.html?redirect).

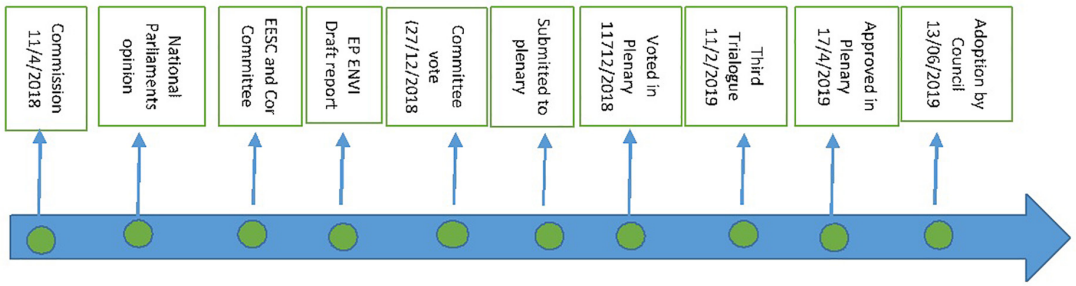

FIGURE 2 | Procedure on Commission's legislative proposal after it was submitted to EP and Council.

recount of events since the submission of the Commission's proposal to the Council and the EP[38] until the adoption of a new regulation on the transparency and sustainability of the EU risk assessment in the food chain by the Council on 13 June 2019. The Parliament finalized its position by a vote and agreement in the Plenary (11/12/2018) followed by the adoption by the Council (12/12/2018). A provisional agreement was reached at the third trilogue meeting (11/02/2019), and was endorsed in the ENVI committee (20/02/2019). "The provisional agreement sets out that: supporting data and information linked to an application for authorization will be made public by the EFSA after the assessment of the validity of the application unless the applicant proves that this could significantly harm its interest and requests confidential treatment by EFSA. The applicant will be able to file a confirmatory request if s/he disagrees with EFSA's assessment of confidentiality. In this case, the information cannot be made public until a final word is said. The Commission will be able to request EFSA to commission its own verification studies in exceptional controversial cases of high importance for the society and member states will have a more active role in helping EFSA attract more and the best scientists to participate in Scientific Panels. Risk communication among all actors – the Commission, EFSA, member states and public stakeholders – will be improved to ensure a more coherent, transparent and continuous flow of information throughout the risk assessment process[39]." The Parliament approved the agreement (17/04/2019) and the Council has formally adopted a new Regulation[40] on the transparency and sustainability of the EU risk assessment in the food chain on June 13, 2019 based on the Commission's proposal[41].

The new Regulation amends the GFL Regulation and eight legislative acts dealing with specific sectors of the food chain: GMOs (cultivation and for Food/Feed uses), feed additives, smoke flavorings, food contact materials, food additives, food enzymes and flavorings, plant protection products and novel foods[42]. Following its entry into force 20 days after publication, September 6, 2019, it will become applicable 18 months later thus by the end of March 2021. The Regulation introduced one important change with respect to the role of the Member States in the governance of EFSA. When the Regulation will apply, each Member State will nominate a representative to the Management Board, increasing their role and level of responsibility in supporting EFSA and ensuring an increased scientific cooperation. The selection of the Member States' representatives in the new Management Board will be based on specific requirements such as relevant experience and expertize in the field of the food chain legislation and policy, including risk assessment. The strict criteria of independence will also have to be fulfilled (ibid).

DISCUSSION

The EU divides the feed and food risk analysis in risk assessment, risk management, and risk communication, where EFSA is responsible for risk assessment, the Commission for risk management and they share risk communication depending if it is an assessment or management issue. This division was a response to the mismanagement of the BSE crisis and the high degree of politicization on food policy, which is today reflected in the rationale behind the governance of EFSA where both the Commission and the Member States instated a "police patrol" type of control. However, this division of competences did not decrease the politicization; at the contrary, it complicated the process by distinguishing the two different levels, one scientific (EFSA) and one political (EC). The scientific committees of EFSA have been criticized for not representing broadly the available scientific knowledge. The agency's work depends on its capacity to combine expertize from the Member States. National scientific organizations contribute to EFSA's work through their participation as experts to EFSA's scientific panels, and by providing EFSA with scientific data and studies.

However, the representation of all Member States in the scientific panels is not required. This was not changed by the recent amendments by Regulation 2019/1381. As a result, only a small number of Member States (six) provide more than two

[38]http://www.europarl.europa.eu/RegData/etudes/BRIE/2018/630315/EPRS_BRI(2018)630315_EN.pdf.

[39]https://www.consilium.europa.eu/en/press/press-releases/2019/02/12/safe-and-transparent-food-chain-provisional-agreement-on-availability-and-independence-of-scientific-studies/.

[40]https://ec.europa.eu/food/sites/food/files/gfl_transparency_comm_proposal_20180410_factsheet_en.pdf.

[41]http://europa.eu/rapid/press-release_MEMO-19-1031_en.htm.

[42]https://europa.eu/rapid/press-release_MEMO-19-1031_en.htm.

thirds of the experts on EFSA's ten scientific panels that can have maximum 21 members[43]. In the last round that started in June 1st, 2018 6 member states (France, Germany, Italy, Netherlands, Spain, United Kingdom) provide 109 out of the 168 experts in the 10 scientific panels of EFSA. Some countries have no representative at any panel, and there are increasing difficulties in attracting enough new candidates to work in them. Here the first difference from EMA that has more financial and human resources and all Member States are represented in the scientific committees. Consequently, the risk assessment process in EFSA by the independent scientists of the scientific committees does not involve all Member States. In praxis, the Member states' different views and interests are expressed and negotiated during the voting in the Standing Committee on the Food Chain and Animal Health under the EC. As a result, although the scientific opinion provided by EFSA constitutes the point of departure for the decisions on the authorization of food and feed, these decisions are strongly affected by national politics and views. When it comes to a highly contentious field such as GMOs and their derived products, the PAFF almost never reach a common decision. There are always a number of EU member states that vote against authorization, despite a favorable scientific recommendation by EFSA (Smart et al., 2015). Looking at the composition specifically of the EFSA GMO panel over the years since its inception, it is obvious that there is a lack of representation from several countries. The panel has had 16–21 experts appointed for 3-year periods. In total, over the periods since 2003 and until the most recent (2018–2021), there has been an accumulated 117 appointments and 72% of these come from only eight countries (**Figure 3**). When this is compared to the voting behavior of these countries in 2003–2015, five of them (Belgium, Germany, the Netherlands, Spain, and United Kingdom) are characterized by a strong inclination to vote in favor of authorization and thus following EFSA's scientific recommendation. Two of them (France and Italy) have a tendency to abstain from voting and occasionally vote either for or against authorization. Several countries that tend to always vote against authorization of GMOs have never been represented in the EFSA GMO panel, such as Croatia, Cyprus, Lithuania and Luxembourg, or represented very few times, such as Austria, Hungary and Poland.

It may be argued that EU Member countries without representation can still be active during the decision making process by submitting their comments and then getting a point-by-point reply afterward in annex to EFSA's opinion. However, the possibility of giving comments does not really compensate for their lack of representation. In fact, this has only created delays, instead of contributing to effectiveness, as countries lacking representation tend to present their own scientific evidence at late stages making the process to start again. In contrast, differences in national opinions regarding the approval of pharmaceutical products are resolved before the EMA provides its scientific opinion to the EC given that all Member States are involved in the risk evaluation as part of EMA's scientific committees.

Any differences in national scientific opinions regarding the approval of pharmaceutical products are resolved before the EMA provides its scientific opinion to the EC given that all Member States are represented in the risk evaluation as part of EMA's scientific committees. Consequently, it is not the long-term credible commitment for common regulation based on scientific evidence, instead, the Member States' short-term interests and politics, which ultimately determine the food regulatory framework. Here the second and biggest dissimilarity. We want to emphasize though that it is important that EFSA remains politically independent and autonomous. Our recommendations do not suggest that EFSA should become politicized. Nor do we suggest that EFSA's scientists should act on behalf of their governments, but rather that representation in EFSA increases the chance that member state being properly and scientifically informed. If an expert from a particular country is member of an EFSA panel, then we believe that the chances increase that the scientific conclusions reach that country's decision makers in a more direct manner (e.g., through personal communications with that expert) and that this will influence the voting behavior in the PAFF, similar to what happens at EMA. At EFSA, the lack of representation is creating a politicized situation in comitology. With the appropriate representation from all Member States all scientific differences in national opinions would be resolved before EFSA provides its scientific opinion to the Commission, who will then basically approve EFSA's opinion as it happens with EMA's opinions.

Moreover, "the regulation of foodstuff mainly has to rely on post-marketing control" because the foodstuff market is much more fragmented with the exception of food additives, as well as novel foods and food ingredients, especially products derived from GMOs, which need to be authorized before they get access to the Single Market[44] (Krapohl, 2004). In contrast, the specific rules for the relatively homogeneous pharmaceuticals products that are produced by large companies allow the premarket[45] evaluation and regulation[46] (Krapohl, 2004), which is another difference in the rules governing the two agencies.

High autonomy and low political influence is what should characterize a regulatory agency. This is relevant for initiatives and collaborations with other regulatory authorities or the industry because the higher the autonomy and the lower the role of politics the more attractive the agency is to collaborate with. However, as explained, the current absence of a long-term credible commitment for common regulation based on scientific evidence is making EFSA a vulnerable target to political interests. If the wish is to have an independent agency able to provide advice based on sound science, several changes have to be made in the organization of the agency.

In the effort to improve citizens and stakeholders confidence in transparency and sustainability of the EU risk assessment, the Commission introduced changes in the legal framework on GFL

[43]https://www.efsa.europa.eu/sites/default/files/event/mb180321/mb180321-i1.pdf.

[44]Sebastian Krapohl, "Credible Commitment in Non-Independent Regulatory Agencies: A Comparative Analysis of the European Agencies for Pharmaceuticals and Foodstuffs," (2004) *ELJ* 5 518, 519.

[45]A post-market control also applies for pharmaceuticals (Pharmacovigiliance), but this works just as a subsequent fire-alarm control.

[46]Krapohl, *supra* note 42, 519.

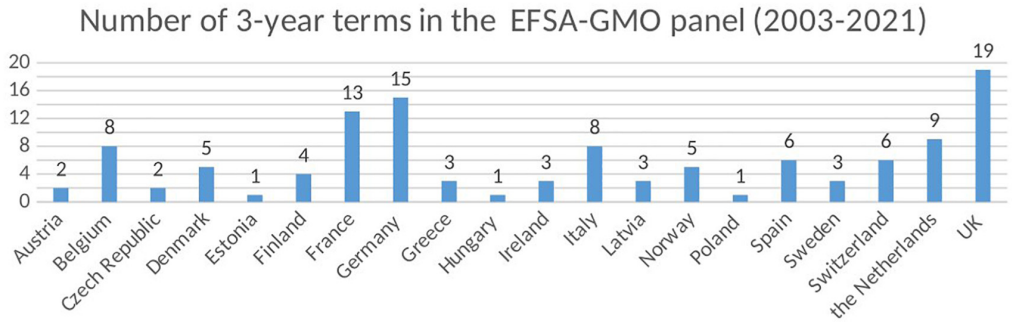

FIGURE 3 | Composition of the EFSA-GMO panels by the EU member states from 2003 to 2021.

BOX 2 | The four main elements of the New Regulation agreement aim at:

- **Ensuring more transparency:** Citizens will have automatic access to all studies and information submitted by industry during the risk assessment process. Stakeholders and the general public will also be consulted on submitted studies. At the same time, the agreement will guarantee confidentiality, in duly justified circumstances, by setting out the type of information that may be considered significantly harmful for commercial interests and therefore cannot be disclosed.
- **Increasing the independence of studies:** The European Food Safety Authority will be notified of all commissioned studies to guarantee that companies applying for authorizations submit all relevant information and do not hold back unfavourable studies. The Authority will also provide general advice to applicants, in particular SMEs, prior to the submission of the dossier. Commission may ask the Authority to commission additional studies for verification purposes and may perform fact-finding missions to verify the compliance of laboratories/studies with standards.
- **Strengthening the governance and the scientific cooperation:** Member States, civil society and European Parliament will be involved in the governance of the Authority by being duly represented in its Management Board. Member States will foster the Authority's scientific capacity and engage the best independent experts into its work.
- **Developing comprehensive risk communication:** A general plan for risk communication will be adopted and will ensure a coherent risk communication strategy throughout the risk analysis process, combined with open dialogue amongst all interested parties.

Source: http://europa.eu/rapid/press-release_IP-19-1030_en.htm

and recently adopted a new regulation based on Art. 43, 114, and 168 (4) (b) of the Treaty of the Functioning of the European Union. The new regulation emphasizes the need for transparency and sustainability of the EU risk assessment in the food chain. The regulation aims to harmonize the procedures followed in the functioning of EFSA with these followed by other scientific agencies such as European Chemical Agency (ECHA) and EMA, since the governance of EFSA is not in line with the Common Approach on decentralized agencies, such as the composition of the Management Board. The specific changes in the functioning of EFSA introduced by the new regulation are going in the right direction (**Box 2**) (points 1, 2, and 4). They can contribute to a more open and qualified communication on risks, which can decrease fear by providing clear information about real versus perceived risks. However, there is space for improvement.

Point 1 on ensuring more transparency: The access of the public to information related to the risk assessment at early stage while ensuring duly justified confidentiality is significant and also relevant to Point 2 on increasing the independence of studies. However, this change combined with the proposed pre-submission procedure, which can be useful especially for small and medium size companies, would require more financial and human resources by EFSA. Another challenge concerns the way it will be justified what requires confidentiality and what not so that it will not threaten innovation and business property.

Point 3 indicates that the new Regulation introduces changes in the governance of EFSA by increasing the involvement of the Member States in the Management Board, and in the nomination of members of the scientific panels, §14 and §15. However, this change focuses on the Management Board that is involved in the administration of finances but not directly in the risk assessment. Besides, this change might increase the number of available qualified risk assessors but it does not address the representation of the member states scientific divergences at an early stage. Consequently, this change does not allow deliberation on scientific divergences among the member states at an early stage, on scientific basis, as it happens in EMA during the risk evaluation. One of the great challenges is how to ensure scientific clarity. This can only happen by having an extended pool of independent scientific evidence and strong collaboration among most, if not all, Member States and the EFSA, which is relevant to Point 2. The need for available tools to support cooperation among between EFSA and the Member States is emphasized by a significant number of respondents[47] (40% of citizens and stakeholders).

Point 4 concerns changes in governance. The main changes linked to the risk assessment process are introduced in Art. 25, Art. 28 (5) and Art.32. Nevertheless, these changes can improve the communication with the public about the relevant scientific evidence used in the risk assessment process, scientific evidence still has important role to play for dispelling widespread misconceptions, so the communication should be science-based and more in a form of public debates as previously

[47] https://ec.europa.eu/social/BlobServlet?docId=21019&langId.

suggested (Qaim, 2016, p. 115). Therefore, there is a need for improvement and simplification of the communication with the public. Better and simpler information by legitimate actors based on scientific facts and democratic principles can shape public opinion positively, beyond biased information and prejudices. It is important for the public to understand how technology can contribute to food safety, food security, and sustainable agriculture development, hence it needs to be utilized and expanded. Biased information and prejudices distorts public opinion.

Unfortunately, the changes introduced by the Regulation do not generate any significant changes with respect to the risk assessment process and the representation of scientists from all the member states, which is crucial for creating trust in public opinion among the member states people. Instead, the amendments mostly focus on increasing and improving communication and openness of the process. Consequently, it is not clear if the new Regulation is able to overcome the existing backdrops, as the governance processes and organization differences are which determine the Commission's final authorization decision.

AUTHOR CONTRIBUTIONS

SC took the initiative and prepared the early draft. All authors made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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REFERENCES

Alemanno, A. (2006). "The evolution of European food regulation – why the European food safety authority is not a EU-style FDA?," in *What's the Beef? The Contested Governance of European Food Safety*, eds C. Ansell and D. Vogel (Cambridge, MA: MIT Press).

Chatzopoulou, S. (2015). Unpacking the mechanisms of the EU 'throughput' governance legitimacy: the case of EFSA. *Eur. Polit. Soc.* 16, 159–177. doi: 10.1080/23745118.2014.974312

Chatzopoulou, S. (2019a). "The food policy of the European union," in *The Oxford Encyclopedia of European Union Politics (Encyclopedia of European Union Politics)* (Oxford: Oxford University Press).

Chatzopoulou, S. (2019b). "The EU agencies' role in policy diffusion beyond the EU: EEA, EMA and EFSA," in *The External Dimension of EU Agencies and Bodies*, eds H. Hofmann, E. Vos, and M. Chamon (Luxembourg: Edward Elgar Publishing).

Christiansen, T. (2019). "Governance in the European Union," in *European Union Politics*, eds M. Cini and Pérez-Solórzano Borragán (Oxford: Oxford University Press), 102–114. doi: 10.1093/hepl/9780198806530.003.0007

Eriksson, D., and Chatzopoulou, S. (2017). Responsible decision-making for plant research and breeding innovations in the European Union. *GM Crops Food* 9, 39–44. doi: 10.1080/21645698.2017.1388496

Eriksson, D., de Andrade, E., Bohanec, B., Chatzopoulou, S., Defez, R., Leiva Eriksson, N., et al. (2019). Implementing an EU opt-in mechanism for GM crop cultivation. *EMBO Rep.* 20:e48036. doi: 10.15252/embr.201948036

Commission Regulation (EU) (2017). *2017/228 of 9 February 2017 Amending Regulation (EC) No 178/2002 of the European Parliament and of the Council as Regards the Names and the Areas of Competence of the Scientific Panels of the European food Safety Authority*. Brussels: EU.

EuropaBio (2016). *GMO Risk Assessment Timelines: is the EU Losing the Innovation Game?* Luxembourg: General Court of the European Union. Available online at: https://www.europabio.org/sites/default/files/INFOGRAPHIC_ASSESSMENT_TIMELINES_v4-Final.pdf

European Court of Auditors (2011). Report on the annual accounts of the European food safety authority for the financial year 2010, together with the authority's replies (2011/C 366/19). *Official J. Eur. Union.* 54, 106–111.

European Food Safety Authority (2011). *Benchmarking of EFSA's Independence – Comparison Between the Tools Ensuring EFSA's Independent Scientific Advice and the Instruments in Use by Organisations Similar to EFSA*. Brussel: Milieu Ltd.

General Court of the European Union (2013). *The General Court has Annulled the Commission's Decisions Concerning Authorisation to Place on the Market the Genetically Modified Potato Amflora*. Luxembourg. Available online at: http://europa.eu/rapid/press-release_CJE-13-160_en.htm (accessed May 4, 2018).

Groenleer, M. (2009). *The Autonomy of European Union Agencies- A Comparative Study of Institutional Development*. Ph.d Thesis, University of Delph, Delft.

Krapohl, S. (2004). Credible commitment in non-independent regulatory agencies: a comparative analysis of the European agencies for pharmaceuticals and foodstuffs'. *Eur. Law J.* 5:519.

Lehrman, A. ed. (2014). *Shaping Our Food – An Overview of Crop and Livestock Breeding*. Uppsala: SLU.

Lehrman, A., Chatzopoulou, S., Feng, C., Forabosco, L., Jonas, F., et al. (2014). *Shaping Our Food - An Overview of Crop and Livestock Breeding*. Uppsala: Mistra Biotech.

Löfstedt, R. (2004). *Risk Communication and Management in the 21st Century*, Working Paper 04-10. Washington, DC: AEI Brooking Joint Center for Regulatory Studies.

Olynk Widmar, N. J., Dominick, S. R., Tyner, W. E., and Ruple, A. (2017). When is genetic modification socially acceptable? When used to advance human health through avenues other than food. *PLoS One* 12:e0178227. doi: 10.1371/journal.pone.0178227

Qaim, M. (2016). *Genetically Modified Crops and Agricultural Development*. London: Palgrave Macmillan.

Sauer, F. (1996). "European medicines evaluation agency: status report," in *Proceedings of the The New Agencies. Conference Report (EUI Working Paper RSC 96/49)*, ed. A. Kreher (Florence: EUI), 23–27.

Smart, R. D., Blum, M., and Wesseler, J. (2015). EU member states' voting for authorizing genetically engineered crops: a regulatory gridlock. *GJAE* 64, 244–262.

Wesseler, J., and Kalaitzandonakes, N. (2019). "Present and future EU GMO policy," in *EU Bioeconomy Economics and Policies: Volume II. Palgrave Advances in Bioeconomy: Economics and Policies*, eds L. Dries, W. Heijman, R. Jongeneel, K. Purnhagen, and J. Wesseler (Cham: Palgrave Macmillan).

Wirtz, S. (2017). *The Interplay of Global Standards and EU Pharmaceutical Regulation*. Ph.D. Thesis, Masstricht University, Masstricht.

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