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RESEARCH ARTICLE

Breaking the impasse: Towards a forward-looking governance framework for gene editing with plants

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Societal Impact Statement

The debate in Europe over how to govern novel techniques of gene editing in plants is fast developing into an impasse with actors rapidly consolidating positions on either side of the debate. Such polemic is not good for science nor for public policy if we are to develop the kinds of socio-technical innovations that are needed to harness socially resilient solutions to pressing global societal challenges, such as food security and climate change. We analyze how we arrived at this impasse and explore novel ways to move beyond it.

Summary

- In this paper we examine the controversy surrounding the governance of gene editing in plants in Europe.
- First, we review social science scholarship, drawing lessons from the public controversy over GM crops and foods. Second, we describe the European policy debate on the gene editing of plants with a particular focus on how the debate is framed by dominant actors. Third, we review solutions other countries have sought, and in particular touch on a level-based approval system that Norway is proposing, articulated recently in a Dutch Rathenau Instituut report. Fourth, we introduce frameworks of responsible innovation as a way of aligning innovation trajectories with articulations and negotiations of broader societal values.
- We find that the lessons from the GM debate have been inadequately learnt and that the struggle over whether or not to amend the current GMO Directive has had the effect of reinforcing established positions. As ways forward, we argue that the application of the Norwegian level-based regulatory framework can help move the focus away from assessments on safety to a tiered assessment of socio-economic considerations, and that a framework of responsible innovation can help transform the cultures and practices of research.
- We conclude by setting out some challenges for the plant science community to engage in responsible research and innovation, both to operate as an honest broker and to engage in early, constructive and on-going public dialogue.

KEYWORDS
controversy, gene editing, genetically modified crops, governance, grand challenges, honest broker, responsible innovation

1 | INTRODUCTION

Food security is one of the global grand challenges for the twenty-first century. With a rising world population and a growing demand for food globally, accompanied by the need to protect biodiversity and ecosystems and the mounting threats associated with climate change, it is unsurprising that food security is fast becoming one of this century's most critical challenges for global policymaking. Yet it remains unclear what innovations in the agricultural sciences are required and how best they are to be pursued. On the one hand, as neatly characterized in a 2009 report from the UK's Royal Society, there is the policy discourse arguing for the "sustainable intensification of global agriculture" (Royal Society, 2009, p. 1; see also Godfray et al., 2010; Godfray & Garnet, 2014; Pretty et al., 2010). Arguing from within a global productivist perspective, the challenge is presented as the largely technical one of how to meet this century's demand for food, feed, fiber, and fuel on an area of land that is unlikely to increase in the future but with a global population that will rise significantly at least until the mid–twenty first century. Within this broad frame, novel science and technology are presented as having a primary role to play in meeting these challenges. Novel research methods have, the argument goes, the potential to contribute to food production through forms of genetic improvement, including the genetic modification of crops that have been altered to introduce new and desirable traits.

On the other hand, there is the counter perspective, contradicting the claim that technological manipulation is a prerequisite to increase nature's productivity and to solve major societal challenges, arguing rather that it has been the policy of intensifying agriculture to maximize yields that has contributed most starkly to our current environmental predicament, characterized by soil degradation, siltation, pollution of water, reduced biodiversity, simplification of cultural landscapes, and an ever worsening climate crisis (Stoate et al., 2001). Various civil society organizations and organic farmers therefore warn against a one-sided approach of productivism, which today is expected to be delivered *inter alia* by gene editing. They argue that such a productivist perspective frames the problem of food security as a lack of sufficient quantities of food, rather than as a lack of access and control of food systems (Helliwell, 2017), maintaining that various different nature-inclusive, ecologically and economically sustainable agricultural practices can also achieve increased productivity, and that the best way to respond to the challenge of food security (or what many prefer to call food sovereignty), particularly in low-income countries, is to deploy agroecological principles to develop sustainable agroecosystems that are both productive and biodiversity conserving, and that can be designed to be socially just, culturally sensitive and economically viable (Altieri, 1995, 2002).

In socio-cultural terms, a number of promising innovations in the plant sciences, principally those shaped by the technological paradigm of molecular biology, have met with considerable social and political resistance. The introduction of transgenic genetically modified (GM) crops in particular, has been deeply mired in controversy, polemic and, in some cases, large-scale opposition and resistance. Although the rise of GM crops has been dramatic in recent decades, their uptake has not been the smooth nor universal transition predicted by its advocates. Controversy has been marked even in those countries where approvals have been impressively rapid. All too commonly, the regulation of GM crops has been challenged as inadequate, even biased, and in some settings such as Brazil (Guivant & Macnaghten, 2015), India (Egorova, Raina, & Mantuong, 2015) and Mexico (Carro-Ripalda, Astier, & Artía, 2015), the planting of certain GM crops has been at times legally suspended. While in other regions such as Europe, governing bodies have struggled to resolve the dilemma of how to stimulate the development of biotechnological innovation for the benefit of the economy and the environment while maintaining public legitimacy. In the next section we examine what lessons can be drawn from the GM controversy. For, unless we arrive at better understandings as to why the governance of GM crops continues to evade policy resolution, attempts aimed at the genetic improvement of crops risk generating further controversy, misunderstanding and polemic.

2 | LESSONS FROM THE GM CONTROVERSY

The social science literature on the GM crop and food controversy includes analysis from the perspectives of particular nation states as well as from a comparative perspective. From the literature one can highlight three dynamics. First, the revolutionary promises that were claimed for the technology by its early promoters—that GM technology would help the poor, alleviate poverty and hunger, address nutritional deficiencies, help feed the world, contribute towards sustainability, and provide better quality food—were not reflected in practice, at least with regards to the outcomes of the first generation of GM crops in the late 1990s and early 2000s (Conway, 1999; Lipton, 2001). The two main types of GM crops that currently dominate the market—those that have been rendered herbicide tolerant (HT) through the insertion of novel genes that code for resistance to the toxic effects of a herbicide (most often Roundup or Liberty herbicides), and those that have been rendered insect resistant (IR) through the insertion of novel genes that code for insect resistance (or stacked variants of IR and HT)—were not designed explicitly with the aim of producing environmental or health or consumer benefits

(ESRC, 1999). Both technologies were aimed to help the large producer and can be considered to be mechanization technologies, enabling farmers to reduce labor costs and to farm larger acreages of crops, such as soya and maize (Buttel, 2005). The inflation of expectations by promising the potential of new biotechnologies to meet societal challenges such as world hunger (Brown, 2003), although important to mobilize resources, not only fed into the concerns of already sceptical civil society groups and nongovernmental organizations (NGOs), but also led to disappointments, and potentially came at the cost of enduring trust relations between society, scientists and policymakers.

The second factor lay in the restricted scope for public and stakeholder involvement in the regulation of GM crop technologies, and in the lack of formal consideration of non-scientific socio-economic or ethical considerations in assessment processes. Technologies have been promoted on economic grounds, with the market as the arbiter, with regulation viewed as a technical consideration, conducted by case-by-case scientific risk assessment that addresses specific harms to health and the environment (Grove-White, Macnaghten, Mayer, & Wynne, 1997). Thus, from the outset, questions concerning the socio-economic, ethical and wider ecological impacts of the technology—including how they would be distributed and how they might impact on public values and smallholder livelihoods—have been excluded as *bona fide* questions within a strictly risk-based regulatory framework (Jasanoff, 2000). An appeal to scientific evidence to convince society on the public value of genetically modified organisms (GMOs)—as with other sociotechnical issues such as the extraction of shale gas (Williams & Macnaghten, 2019; Williams, Macnaghten, Davies, & Curtis, 2017)—repeatedly has been shown to be inadequate, because scientific evidence on harms does not exhaust the issues that society deems to be important (Wynne, 2001; for a wider argument on the limits of regulatory science and their chosen methodologies for determining policy on GM cultivation, see Wickson & Wynne, 2012). Broader concerns of citizens need to be addressed in the discussions, and communities and NGOs need to be included from the onset to avoid any intensification of controversy (Kearnes, Grove-White, Macnaghten, & Wilsdon, 2006). In the Global South in particular, the uptake of GM crops has been associated with the widespread adoption of neoliberal policies aimed at the institutional reform of agriculture. Keenly advanced by international organizations—including the World Bank, the World Trade Organization (WTO), the International Monetary Fund (IMF), and the World Intellectual Property Organization (WIPO)—a global legal and regulatory regime has been developed based on ideals of market liberalization, free trade, intellectual property rights, and harmonized approaches to risk assessment (Busch, 2010). Importantly, the seed companies themselves have promoted a restrictive approach to the regulation of GM crops across multiple jurisdictions, often invoking international trade rules, where social need is equated to that of the free choice of consumers in the marketplace, and where the scope of regulation is restricted to cover solely the scientific evidence of harms rather than the appraisal of its contribution to the social good (Newell & Glover, 2003).

The third factor arose from the evolution of different approaches to regulation. In the United States, a regulatory regime emerged that considered genetic engineering as a process that presented no special risks that could not be addressed by existing product-oriented legislation (National Research Council, 1989). This led to the principle of "substantial equivalence" that came to govern international trade policy, including that of the WTO (Murphy & Levidow, 2006). In Britain and later in Europe, a more expansive view of the potential for GM technologies to generate harm developed, including those surrounding the industrial production of GMOs and their deliberate release. Here, a regulatory system developed in which the process of genetic modification became an appropriate basis for determining policy (Jasanoff, 1995). This disjunction in EU versus. US regulatory frameworks provided an "opportunity structure" for NGOs—and later other actors including the media—to operate at the interface between governments and concerned publics, helping to define the issue as a public issue through appealing to the technology as an imperial and colonizing force and of resistance (e.g., through consumer boycotts and the theatre of protests) as "a symbol of the environmental, economic, and cultural homogenization they wished to resist" (Jasanoff, 2006:284). The different regulatory frameworks did not create the controversy directly; rather, they facilitated an operating space for NGOs (and later, the media and other actors) to translate "diffuse or unfocused public concerns into terms compatible with what they understand to be the particular policy world in question" (Grove-White, 2001:469). While arguing within the parameters of risk and precaution to governments and regulatory bodies (this was the only tractable discourse available), NGOs mobilized public support through a range of broader arguments: that GM foods would lead to an inevitable loss of consumer choice, that decisions had already been taken outside the public sphere, that GM crops would lead to the corporate control of food systems, that GM crops and foods would benefit only multinationals and large-scale farmers, that the technology was "unnatural" and that there would be probable unpredicted effects beyond the reach of risk science. Importantly, these arguments, which were identified as "latent" and cross-cutting societal concerns even before the controversy took hold (Grove-White et al., 1997; see also Marris, Wynne, Simmons, & Weldon, 2001), were simply not captured by the formal and technical language of safety and risk. One effect of this omission was to make debates over the risk and safety of GM crops stand-in for a host of other unacknowledged concerns (Frewer et al., 2004; Gaskell et al., 2004). Yet the intensity of these wider concerns was reinforced by the lack of official assurances of the adequacy of current regulatory assessment mechanisms (Kearnes et al., 2006).[1]

[1]In this section we have focused on two regulatory regimes, the EU and the US, because this distinction is emblematic of a wider schism that is playing out globally. Other jurisdictions have tended to adopt a US product-based model (Canada), a combination of process (EU) and product-based (US) models under general laws on biosafety (Brazil, Argentina, Mexico) or more pragmatic approaches that emphasize to the economic interest of a given application (China) (see Nap, Metz, Escaler, & Conner, 2003). On the influence of global regimes, and in particular the Cartigena Protocol on the regulation and subsequent cultivation of GM crops across a variety of domestic contexts, see Gupta & Falkner, (2006).

In this section we have articulated three factors that help account for the controversy of agricultural GM technologies and the forms that it took. Importantly, these factors transcend the question of risk and thus point to dynamics where the provision of scientific information on harms have done little to provide socially robust governance. It also points to lessons for the future development of GM crops: not only do GM crops and foods need to demonstrate a benefit, either a local consumer benefit and/or a contribution to societal challenges, but the framing of benefits needs to align with articulations of societal values. Crucially, it is important that benefit analysis includes a socio-economic assessment of how a GM crop impacts on questions of access (the extent to which the crop improves or not access to food, particularly for vulnerable populations), control (the extent to which farmers, citizens and consumers exercise control of the agricultural and food system), and the public interest (defined as the extent to which the crop contributes to the public good) (see Nuffield Council, 2012). For example, while recent GM crops such as non-browning *Arctic Apples* and reduced bruising *Innate Potato* may claim to demonstrate consumer and societal benefit, narrowly defined in terms of delivering less waste and thus contributing to sustainability goals, it is less clear whether these crops have been designed primarily to benefit farmers or consumers, as opposed to say supermarkets and supply chain intermediaries who will have a longer lease on product life (Rommens, 2018), let alone designed to impact on the systemic problems associated with food vulnerability. In the next section, we describe the current debate on gene editing in Europe, demonstrating that the current discourse in important respects follows a similar pattern as was the case for GMOs.

3 | FRAMING THE DEBATE ON THE REGULATION OF GENE-EDITED PLANTS[2]

New techniques have been developed in the last few decades aimed at solving a number of existing problems of the classic recombinant DNA technology that has been used to create GMOs.[3] For these reasons, gene editing has been rapidly taken up in diverse fields both in laboratory science and in policy deliberation. In this section, we examine how the debate on regulation and governance has been framed in Europe up until the time of writing (January 2020). With the new gene editing technologies, it is possible to make small, targeted changes to the genome in the laboratory, without having to insert foreign DNA into the gene. This has intensified the debate as to whether the European GMO Directive does and should apply to this and other new breeding techniques. As a historical narrative, agrochemical breeding companies and various knowledge institutions have tended to argue that it has been time consuming and expensive to apply for a licence for GM crops in Europe, and that this has had the effect of hampering innovation. The debate on whether gene-edited crops are GMOs should be seen in this light: exempting gene editing from the Directive could have significant economic implications. For this reason, much of the debate on gene editing in Europe is shaped by, and centered on the current regulatory framework, including the question as to whether gene-edited crops should be exempted from the European GMO Directive.

To begin, it is important to clarify some issues regarding the current regulation, in order to avoid misinterpretation. The European GMO Directive 2001/18/EC does not prohibit the cultivation of GMO crops, but regulates the release of GM crops into the environment. The aim of the scientific-based licensing procedure is to ensure a high level of protection of human life and health, and of the health and wellbeing of animals and the environment. Crops subjected to the GMO Directive require an Environmental Risk Assessment (ERA); they will be monitored; and under Directive (EC) no. 1830/2003, traceability and labeling is ensured, with the aim of informing consumers. Non-GMO crops (as well crops bred with conventional mutagenesis methods which are exempt from the Directive) are required to undergo tests only for distinctness, uniformity and stability (DUS-testing), and for value for cultivation and use (VCU). However, the DUS and VCU testing do not contain any environmental or health risk assessment. Nor does the public have an opportunity to take part in the decision-making process, in contrast to new GMO varieties, where member states are required to consult the public (Article 9 of the GMO Directive) (Habets, Hove, & van Est, 2019).

Agrochemical and plant breeding companies, as well as many research institutes, have argued that gene editing can and should be viewed as a modern form of mutagenesis.[4] And because traditional mutagenesis is exempt from the GMO Directive, the new gene-editing techniques should also be exempt, so long as no foreign DNA is present in the end product. Moreover, according to them, this new method of mutagenesis is more accurate than traditional mutagenesis methods—which involve exposure to radiation or chemical mutagenesis—and is therefore safer. The claim that gene editing-induced changes are similar to what may occur naturally is however, presently, still an untested hypothesis (Sustainable Pulse, 2020). Nor is "more accurate" synonymous to safer; this claim of safety disputed as gene-editing techniques are still in their infancy (Habets et al., 2019). IFOAM Organics International (2016) have highlighted the discrete steps that are necessary in the gene editing process[5]—

[2]Sections 3 and 4 are informed by research conducted by one of the authors, MH (see Habets et al., 2019).

[3]With this older form of genetic engineering, it was, for example, difficult to position a desired change at an exact location in the DNA of the host organism. Genome editing techniques offer a solution to this problem, the most promising of which is the clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9 (CRISPR-Cas9) system, which consists of a guide RNA, designed to find and bind to a specific sequence in the DNA, and the Cas9 enzyme which, after binding, can be used as scissors to cut specific sequences. By adjusting the accompanying guide RNA, the CRISPR-Cas9 complex can be used to cut the DNA at any location. The DNA is then repaired by the cell itself, allowing for modifications in the DNA sequence. Crispr-Cas9 has allowed for the altering of genetic material to become quicker, easier, more specific, more versatile, and more accessible.

[4]Gene-editing *can* be used to make small changes within the genome; however, it can also be used, *inter alia*, to integrate large (or small) chunks of foreign DNA into the genome. The debate in Europe has been dominated by a debate on the status of gene editing applied to changes within the genome, notwithstanding the plurality of possible uses.

[5]In addition, for specific, targeted changes in the DNA, cells need to be induced to enter a particular stage in the cell cycle in order for the cell to use homology directed repair instead of the non-homologous end joining DNA- repair mechanism of the cell.

for example, cultivating the cells, preparing the cells, the transformation, the transfer of method-related components into the recipient cells, the insertion of the DNA template, methods to regenerate modified plants from single cells etc.—all of which carry risks due to changes at the genetic and cellular level (Braatz et al., 2017; Eckerstorfer, Dolezel, et al., 2019; Ladics et al., 2015; Lathan, Wilson, & Steinbrecher, 2006; Mehrotra & Goyal, 2012). Indeed, even small changes at the genetic level can lead to major changes at the level of an organism. For example, the transition from the prostrate growth of ancestral wild rice to the erect growth of rice cultivars, one of the critical events leading to the domestication of rice, is the result of a single mutation in the PROG1 gene—a small change at the molecular level but with substantial consequences (Tan et al., 2008). Besides, unintended effects of targeted genetic modification, such as pleiotropic effects, are well-known (Eckerstorfer, Dolezel, et al., 2019). For example, a number of pleiotropic effects, including reduced plant size, and premature senescence have been found in a gene-edited plant made resistant to powdery mildew, a fungal disease (Kusch & Panstruga, 2017).

Furthermore, an exemption for gene editing in the regulation would not only constitute an exemption for current techniques like CRISPR-Cas9, but also for other gene editing techniques being developed now and in the future. Given that research increasingly appears to be demonstrating the drawbacks of this "relatively unpredictable and blunt form of molecular scissors that cut sizeable sections of DNA" (Dolgin, 2017:439), this is viewed as a troubling scenario. Challenges of the CRISPR-Cas9 system, are amongst others, (a) unintended mutations in other parts of the DNA (see Fu et al., 2013; Marx, 2014; Peng, Lin, & Li, 2015; although these so-called off-target effects can also occur in unregulated classical mutagenesis processes); (b) unintended large deletions of DNA and more complex genomic rearrangements (Kosicki, Tomberg, & Bradley, 2018); and (c) unintended molecular changes near the intended site of the modification (Kosicki et al., 2018). Disquieting is the recent observation of US Food and Drug Administration (FDA) researchers that the current standard screening methods for gene-edited products have a potential blind spot (Norris et al., 2020).

Currently, there remain knowledge gaps and bottlenecks needed for the effective use of gene editing for crop improvement (Vats et al., 2019). NGOs and the European Network of Scientists for Social and Environmental Responsibility (ENSSER) emphasize that scientific knowledge on the short-term safety of gene-edited products is limited (ENSSER, 2017). And even if we were to have this data, the application of the precautionary principle would still require these techniques to be regulated, due to the absence of information on *long-term* safety.[6] More widely, there are concerns that the likely political economy of gene-edited crops in practice may exacerbate the ecological impacts deemed to be associated with GM crops, leading to a reduction in genetic heritage and biodiversity, a reduction in seed diversity, and the extension of monocultures (IFOAM Organics International, 2016, 2017).

In 2016, the highest administrative court of France, the Conseil d'État, asked the European Court of Justice to clarify the scope of the GMO Directive and the scope of the exemption, following a claim made by Confédération paysanne—a French agricultural organization representing the interests of small-scale farms—along with eight environmental associations, that some plants made tolerant to herbicides with new breeding techniques were exempt from the EU GMO Directive. On 25 July 2018, the Court clarified the interpretation of the applicable law judging that all organisms altered by mutagenesis methods or techniques are genetically modified organisms according to the GMO Directive (CJEU, 2018). The ruling determined, therefore, that all products of genome editing are subject to the European GMO Directive, with the exception only of certain methods that had "conventionally been used in a number of applications and [that] had a long safety record" (Annex 1B). This legal interpretation of the GMO Directive has been understood, and criticized by many, as if it is a political statement of the Court of Justice. At the 2019 CRISPRcon meeting in Wageningen, for example, some even went so far as to call the ruling anti-science (Arora, van Dyck, & Wakeford, 2019). As a consequence of the ruling, proponents for exempting gene editing from the Directive are now urging member states to persuade the European Commission to address this subject in the next five years. Either actively or passively, the European Commission will have to make a political decision on how Europe will regulate gene-edited crops in the coming years.

On the one side, the agrochemical and plant-breeding companies, and associations such as the European Academies Science Advisory Council (EASAC), the European Seed Association, EuropaBio, and Plantum, present two kinds of arguments for an amendment (Michalopoulos, 2018; Plantum, 2019): first, they warn of the economic and reputational consequences for Europe if it does not change the current regulation, with agrochemical and seed companies, as well as scientists, moving to countries where regulation is more lenient, leading Europe to fall behind, with reduced national capacity and a loss of scientific credibility. Second, they forewarn ecological consequences, with reduced capacity for Europe to develop the innovations necessary to solve some of the major global societal challenges, such as food security and climate change. Other complications and trade-offs are also associated with the GMO Directive not being amended. These include: the costs associated with having to label imported gene-edited foods (to ensure freedom of choice), the possibility of a trade dispute arising with countries with non-regulated foods, the difficulty of detecting foods without foreign DNA, the stifling of innovation, and the fear of being left behind.

On the other side, civil society and NGOs emphasize that if Europe decides to amend the Directive in order to exempt the new techniques, it will have failed to draw the lessons from the GMO controversy, notably the wider socio-economic, political and ethical factors that underpinned the controversy, and that are equally likely to arise with gene-edited foods and crops. Just as with GM

[6]The precautionary principle, a fundamental principle of European legislation, alongside the precautionary approach, as formulated in the Cartagena Protocol on Biosafety to the Convention on Biological Diversity, seeks to ensure that appropriate measures are taken in advance to avoid adverse effects on human health and the environment.

crops, gene-edited crops have the propensity to exacerbate power imbalances, to reinforce the current monopoly position of existing seed companies at the expense of vulnerable small-scale farmers, and to fail to make meaningful contributions to the world's pressing problems. As illustration, two early patents in gene-edited organisms are for non-browning mushrooms and for grass that requires less mowing, consumer innovations that are hardly going to contribute in substance to meeting the world's global challenges (Habets et al., 2019). Furthermore, should gene-edited crops be exempted from the European GMO Directive, these crops will not require labeling, thus in conflict with Directive (EC) no. 1830/2003, that guarantees traceability and labeling, with the aim of informing consumers. Crops exempt from the Directive are thus not only exempted from risk assessment and monitoring requirements, but also from traceability and labeling. To summarize, in the current European policy debate the contrasting positions of two sets of actors reflect established positions, and are shaped by dominant policy discourses that revolve around safety, precaution and the economic importance of innovation.

4 | A WAY FORWARD

Europe is not alone in her struggle to search for appropriate regulatory oversight of this second wave of genetic modification techniques. Different countries are opting for different approaches, depending on the existing oversight of both conventional and GM crops. In the United States, oversight of GM plants as well as conventionally bred plants lies with three US governmental agencies: the United States Department of Agriculture's Animal and Plant Health Inspection Service (USDA–APHIS), the Environmental Protection Agency (EPA), and the Food and Drug Administration (FDA).[7] In March 2018, the USDA issued a statement declaring that it will not regulate plants under its biotechnology regulations if they are developed with new breeding techniques that could otherwise have been developed through traditional breeding techniques, provided they are not plants pests or developed using plant pests (USDA, 2018). Consistent with this statement, and in line with the Trump administration's wider pro-innovation, reduce–regulatory burden policy narrative (Kuzma, 2019; Montenegro de Wit, 2020), in June 2019 the agency proposed a draft rule, providing developers with the option to self-determine whether their gene edited plant variety is exempt from regulation and to request written confirmation from the agency that the self-determination is valid. The FDA is currently working on a clarification of its approach to gene-edited plant-derived foods. Gene-edited crops that are insect or disease resistant are evaluated by the EPA, who are currently evaluating whether some existing exemptions also apply to gene-edited products, and considering approaches to clarify the regulatory status of this (Friedrichs et al., 2019). The regulatory oversight in the US is therefore still pending.

In New Zealand, the government has decided that for the moment, all gene-edited applications are regulated according to the national biosafety framework (Eckerstorfer, Engelhard, Heissenberger, Simon, & Teichmann, 2019). In contrast, Australia has opted not to subject gene-editing techniques to the Gene Technology Act 2000 provided no new genetic material is introduced (Mallapaty, 2019). This entails that products modified with gene-editing techniques are not GMOs, when no template containing genetic material to direct the repair process (non-homologous end joining) is used to repair the break, a process that more closely resembles mutagenesis, as here too, the cell amends the break without added templates of nucleic acids. However, with regards to specifically gene-edited foods, Australia is still considering how to regulate. Japan will not regard organisms without remnants of inserted nucleic acids (template) as Living Modified Organisms (LMO), when considering their release to the environment. However, information has to be submitted to the relevant authorities (and to be made public, bearing confidentiality considerations) on aspects that include, the method used, the trait changed, the modified gene, and its function, and a discussion of the possible influence on biological diversity when the organism is used (Ministry of the Environment, 2018). For food derived from genome editing technologies, the Ministry of Health, Labour and Welfare would determine on a specific case-by-case basis whether a notification or safety assessment is required (Ministry of Health, Labour, & Welfare, 2019). Genome-edited products intended to be placed in the market need to undergo a prior consultation.[8]

While the methods of regulatory oversight of the US, New Zealand, Australia and Japan may respond to some of the public concerns regarding the risks of gene editing in plants, they do not confront the broader socio-economic and environmental considerations, or concerns, that we view as necessary for robust governance. In Norway, by contrast, the Norwegian Biotechnology Advisory Board (Bioteknologirådet, 2018) has set out a forward-looking regulatory framework aimed at harnessing the potential of gene technology, while at the same time protecting health and the environment, and promoting societal benefit, sustainability and ethics. Norway is uniquely placed to integrate such considerations into a regulatory framework. Since 1993, the Norwegian Gene Technology Act has stipulated that the production and use of genetically modified organisms takes place in an ethical and societally responsible manner, in accordance with the principle of sustainable development and without harmful effects to health and the environment. Broader socio-economic and sustainability considerations have thus been integrated into a biotechnology regulatory framework over a

[7]The FDA instigates a voluntary consultation process to determine whether a new GM food would require premarket approval. The USDA regulates conventional and GM-organisms and products that are known or suspected to be plant pests or to pose a plant pest risk. And the EPA regulates the sale, distribution and use of pesticides in order to protect health and the environment, including regulation of those pesticides that are produced by GMOs (USDA, 1986).

[8]In this section, we have described how various countries have taken different decisions on the regulation of new gene editing. For an overview of different regulatory decisions on plant gene editing by various nations, see Eckerstorfer et al., (2019b) and Friedrichs et al., (2019).

longer period, and in a more holistic manner, more than in any other jurisdiction.

The Norwegian Biotechnology Advisory Board recommends a differentiated approach, arguing that not all GMOs should be regulated equally, as in the current system. An example of a possible method is as follows: for changes that are temporary, and with non-heritable changes (Level 0), these would be exempt; for changes that can exist or that can arise naturally, and that can be achieved using conventional breeding methods (Level 1), a notification to the relevant authorities would be sufficient; for changes that involve genetic changes within the same species that could not be achieved using conventional breeding methods (Level 2), there would be an expedited risk assessment and approval requirement; while genetic changes that cross the species boundary, or that are introduced from synthetic (non-naturally occurring) DNA (Level 3), these would be subject to the current standard assessment and approval system. And, as with the current assessment regime in Norway, all GMOs would need to be assessed in relation to their contribution to societal benefit, sustainability and ethics; criteria that are also recognized as important in the EU Directive 2015/412. Traceability and labeling will remain a formal requirement, thus providing consumers freedom of choice. The Norwegian model could serve as an example for the EU, and it could make an important contribution to breaking the impasse, as it engages in a serious manner with the arguments of both proponents and opponents as set out in Section 3 above. The advantages to such a tiered system are considerable in that they offer in principle a way of linking risk assessment with an assessment of benefits, of relaxing the current regulatory regime only in the context of agreement on societal benefit, sustainability and ethics, and ultimately a model designed to harness the potential of gene technologies while responding to significant societal concern and unease.

Undoubtedly, there remain a host of unresolved issues associated with a change in the regulation and oversight of biotechnology to a level-based approach designed to take into account broader societal and environmental implications: for one, it is challenging to operationalize the criteria of societal benefit, ethics, and sustainability. Although the Norwegian Biotechnology Advisory Board has worked out parameters for these criteria in several reports (Bioteknologirådet, 2009, 2011, 2014), in practice Norway has never had to evaluate GM crops based on these broader considerations.[9] In addition, the question of who, and with what competences decisions would need to be made needs serious consideration. Answering these questions (and more) requires deliberative and consultative debate with stakeholders, alongside institutional experimentation, and ultimately legislation.

[9]Current documentation required to secure market approval of GMOs by the EU does not contain sufficient information to assess these broader criteria. The additional information that Norway would require for approval has also so far never been requested, as no applications have been made by companies, largely due to the fact that the Norwegian market is small, and therefore not deemed the additional effort by companies.

5 | A FRAMEWORK OF RESPONSIBLE INNOVATION

If we are to govern gene-edited plants and ensure these are aligned with societal needs and values, we need more than institutional redesign, important though this is. For responsible governance, not only do policymakers have to address the wider ethical and societal implications of gene editing; there also remains the need to increase the scope for public and stakeholder engagement *and* to transform the cultures and practices of research, starting with the plant science community. In this section we set out a framework of responsible innovation as providing a set of tools—and ways of thinking—about such transformation.

Responsible innovation is a science policy discourse that has been gaining traction in Europe in recent years, which we have defined elsewhere as "taking care of the future through collective stewardship of science and innovation in the present" (Stilgoe, Owen, & Macnaghten, 2013:1,570; see also European Commission, 2013; Owen, Macnaghten, & Stilgoe, 2012; von Schomberg, 2013). To operationalize this definition, four dimensions of responsible innovation were derived —anticipation (A), inclusion (I), reflexivity (R), and responsiveness (R) (the AIRR framework)—that provide a framework for raising, discussing and responding to questions pertaining to the broader impacts of science and technology. These dimensions are important characteristics of a more responsible vision of innovation, which can, it is argued, be heuristically helpful for decision-making on how to shape science and technology in line with societal values.

Anticipation is the first dimension. Anticipation prompts researchers and organizations to develop capacities to ask, "What if…?" questions, to consider contingency, what is known, what is likely, what are possible, and plausible impacts. This entrusts the research community to identify and appraise the possible and plausible future impacts of diverse research and innovation pathways. Such a task is fraught with epistemic complexity as one moves beyond simple, deterministic notions of risk to embrace wider socio-economic and ethical-cultural considerations (Barben, Fisher, Selin, & Guston, 2008; Guston, 2014; Ludwig & Macnaghten, 2019). When applied to the practice of gene editing in plants, research in genomics and nanotechnology has shown that researchers have in the past made over-optimistic promises of major beneficial social and industrial transformation, and that these promises have been made not simply to predict but also to shape desirable futures—by attracting interest, leveraging funding and forming agendas (Borup, Brown, Konrad, & van Lente, 2006; Brown & Michael, 2003; Brown, Rappert, & Webster, 2000; Fortun, 2001; Fujimura, 2003; Hedgecoe & Martin, 2003; Selin, 2007). This suggests a need for what Fortun (2005) calls "an ethics of promising", to instill responsibility in the research community by disentangling present hype from future reality. In addition, given that at least 1st generation GM crops have been developed and adopted throughout much of the developed and developing world, an anticipative approach requires a systematic contextualization of GM crops' social and ethical impacts, as a

precondition for imagining how gene-edited crops could be otherwise configured. That is to say, a better understanding of the context out of which GM crops developed is required, of the kinds of social worlds they have contributed towards, and thus, by implication, of how such contexts may need to be reconfigured if gene-edited crops (and associated developments in the crop sciences) are to contribute to more inclusive, socially just and environmentally sustainable futures (Macnaghten, 2016).

Inclusion is the second dimension. Associated with the historical decline in the authority of expert, top-down policymaking and the inclusion of new voices in the governance of science and technology, researchers and organizations are asked to engage in early and two-way deliberation with a wide range of stakeholders and publics on the visions, impacts and broader socio-economic questions associated with particular research and innovation initiatives (Wilsdon & Willis, 2004). Partially, such inclusion seeks to facilitate the articulation of new meanings through deliberation on the distinctive set of social, economic, political and ethical questions that a new technology may bring into being, and partially to open up the framing of issues that may challenge entrenched assumptions and commitments. The forms of inclusion are multiple, ranging from small-group processes of invited public dialogue in the form of focus groups, consensus conferences, deliberative mapping, and citizen assemblies—what Goodin and Dryzek (2006) call mini-publics—to innovations in more formal governance arrangements in the form of multi-stakeholder partnerships, citizen forums, the inclusion of lay members on scientific advisory committees, user-centered design, and other hybrid mechanisms (Sykes & Macnaghten, 2013). To mitigate against the use of public participation as legitimation, Callon, Lascoumes, and Barthe (2009) have offered criteria that represent indicators of good practice: intensity—ensuring that publics and stakeholders are consulted early in the innovation R&D process; openness—ensuring that a diverse and inclusive array of groups are represented; and quality—ensuring that the discussions and deliberations are conducted in a serious and continuous manner.

Reflexivity is our next dimension which we define—at the level of individual and institutional practice—as the practice of "holding a mirror up to one's own activities, commitments and assumptions, being aware of the limits of knowledge and being mindful that a particular framing of an issue may not be universally held" (Stilgoe et al., 2013:1571). This emphasis on reflexivity in scientific practice is situated in a wider tradition of science and technology studies that has criticized deficit models of public distrust in emerging science and technology (Wynne, 2001, 2006). Rather than interpreting public distrust as an expression of ignorance towards relevant facts, this literature emphasizes the need for institutional reflexivity arising from the possibility of competing framings, including those that are driven by lay concerns and perspectives. How to embed reflexivity into scientific and science policy culture and practice remains a formidable challenge. Innovations aimed at building reflexivity into scientific practice include practices such as "mid-stream modulation" and "ethical technology assessment", both involving the participation of social scientists and philosophers at the laboratory level (Boenink, Swierstra, & Stemerding, 2010; Fisher, Mahajan, & Mitcham, 2006; Guston & Sarewitz, 2002; Schuurbiers, 2011, while a broader set of innovations are being developed that aim to build reflexivity at the organizational level—into what we might term the wider science governance ecosystem—that includes research funders, regulators, universities, government ministries, and the other science policy institutions (Chilvers, Pallett, & Hargreaves, 2015). To assist in such reflexivity, plant scientists need to demonstrate, inter alia, greater sensitivity to the relationality that exists between people and land, to the mechanistic and reductionist frame that commonly exists in crop science laboratory practices, and to the impacts posed by the neoliberal collectivization of global agriculture on questions of human freedom, dignity and sovereignty (Harvey, 2015; Northcott, 2015).

Responsiveness is our fourth dimension, requiring research managers and science policy organizations to develop capacities to focus questioning on the three dimensions listed above and to change shape or direction in response to them. This demands the development of policy and governance mechanisms aimed at the practical implementation of responsible innovation as well as openness and leadership within science policy organizations to facilitate the empowerment of social agency in technological decision-making. It must also be responsive to the wider national and international political context shaping science policy initiatives. On the one hand, we can point to a growing wave of science policy initiatives that contend that a central challenge of responsible innovation is to become more responsive to grand societal challenges (Lund Declaration, 2009; von Schomberg, 2013). But such challenges are not preordained, nor are they uncontested, and an unreflexive use of a grand challenge discourse in research and innovation policy can contribute to shallow operationalizations of responsibility. There are various mechanisms that might allow innovation systems to respond to improved anticipation, reflexivity and inclusion. In some cases, the application of the precautionary principle, a moratorium or a code of conduct may be appropriate. While, in other cases it may be more appropriate to design particular values into technology (van den Hoven, Vermaas, & van de Poel, 2015), or to adopt the use of a stage-gate (Macnaghten & Owen, 2011). Notwithstanding these structural constraints, public research on these matters need to be seen as a strategic priority for the successful governance of gene-edited plants, to experiment with the crafting of new policy architectures, and to develop coherent alternative models of governance should opportunities in the wider polity emerge. In Section 4, we have articulated one specific suggestion for how policy institutions could be more responsive through an innovation in regulation, with a tiered proposal that includes relaxing the current regulatory regime only in the context of agreement on societal benefit, sustainability and ethics. For successful implementation, this demands openness and leadership within science–policy organizations, a key challenge given the rigidities that have characterized the regimes of governance and regulation in current arrangements (Macnaghten & Carro-Ripalda, 2015; Raina, 2015).

Moving beyond the range of processes described above that seek to advance single or multiple dimensions, responsible innovation demands their integration and embedding in governance. The

dimensions do not float freely but must connect as an integrated whole. It is necessary to draw connections both between the dimensions and with the contexts of governance in which they sit to enable them to be embedded in particular institutional contexts and to be adjusted to take into account local idiosyncrasies. Developing a coherent integration will be critical if we are to move beyond the current impasse in Europe. Only as an integrated whole can responsible innovation help address the question of "what kind of society we want to be" and more generally accomplish its mission of "taking care of the future through collective stewardship of science and innovation in the present".

6 | CONCLUSION AND DISCUSSION

In this paper we set out a forward-looking governance framework for gene editing with plants. We argued that if innovations in the plant sciences are to fulfil their potential in contributing towards the global grand challenges of the twenty-first century they need to be developed with and for society. We then outlined four core elements for how this can be accomplished. First, in Section 2 we highlighted the need to learn lessons from the GM controversy, namely, to ensure that the radical promises of gene technology are realized in practice, that there is scope for broad inclusion of publics and stakeholders in regulatory processes, and that we recognize how debates over the risks and safety of gene-edited crops and foods can stand in for a host of wider unacknowledged socio-economic and ethical concerns. Then, in Section 3 we reviewed the current debate on the regulation of gene-edited crops in Europe, finding not only that lessons from the GM controversy had been inadequately learnt but that the struggle over whether or not to amend the current GMO Directive had reinforced established positions and mobilizations. Subsequently, in Section 4 we reviewed how different countries are opting for different approaches to regulation, including a Norwegian proposal for a policy option for a level-based regulatory framework that moved the focus away from arguments on safety to a tiered assessment of broader socio-economic considerations, as a means of breaking the current rigidity of debate on the GMO Directive. And finally, in Section 5 we set out a framework of responsible innovation as a tool and an approach to transform the cultures and practices of research.

We conclude with a few summary remarks. First, our broad aim in this paper has been to broaden the debate on governance away from a narrow technical discussion of risks and off-target effects to a wider societal conversation on the stakes underpinning a move into gene-edited crops and foods. What we have sought to describe are some of the key elements of a more substantive account of the socio-economic and ethical issues that need to be addressed and some of the processes for addressing them. Engaging these questions with scientific, corporate, civil society, public, and government actors is both needed and potentially transformative, for example, by contributing to more responsive decision-making processes, by enabling scientists and companies to better integrate ethical and socio-economic concerns into their strategy and practices, and by enabling governments to discuss policy and regulation with more dynamic and socially reflexive concepts. How such a framework can be put to use in the European context will require innovation and leadership. The European Commission has actively promoted responsible research and innovation (RRI) in its framework programmes and it would be highly plausible for the Commission to operationalize a framework such as that articulated in this paper to help move the debate forward. Of course, such a move would most likely be resisted by incumbent logics, norms, cultures, and institutional practices (Lawrence & Sudderby, 2006), as such a regime may not be in the (short-term) interests of actors at both sides of the debate, as described in Section 2 above.

Into such a heated atmosphere it is critical that the plant science community enters into a serious conversation as to its role and responsibilities. New plant biotechnologies offer potential for good and harm, and when a wider set of socio-economic considerations are proposed as both *bona fide* and as necessary for governance and oversight—as set out in this paper—we are all forced to confront questions of exceptional difficulty and complexity. In such circumstances, as Glen Stone points out, we urgently need the plant science community to act as "honest brokers, to help educate, enrich debate, and inform policy…[the problem being that] the disciplines most directly related to biotechnology has been a casualty of the last two decades of rhetorical warfare over genetic engineering" (Stone, 2017:584). For Stone, this entails that the plant science community renews its commitments to the Mertonian norms, such as independence, organized scepticism and disinterestedness, and, following Pielke (2007), to use science to expand and clarify a scope of choice, but to allow others to make decisions according to their own values. While the original Mertonian norms are indeed necessary for scientific integrity, these are in need of development and expansion so that they embrace new and more forward-looking norms and values aimed at increasing the capacity of science and scientists to reflect, to include and to anticipate. This does not imply that at least some of the lessons have not been learnt by the plant science community. There are plant science initiatives, such as the OpenPlant Synthetic Biology Research Centre at the University of Cambridge— a joint initiative between the University of Cambridge, John Innes Centre and the Earlham Institute, funded by the BBSRC and EPSRC as part of the UK Synthetic Biology for Growth programme (Open Plant, 2020)—that have internalized some of the lessons of GM by recognizing that at least part of this debate is about ownership of technology. This is a helpful and constructive example of scientists acting reflexively. But to operationalize such forward-looking norms and values in practice will require more profound collaboration between the plant sciences and the social sciences (and the broader humanities), alongside a deep and continuous engagement with societal actors at all stages of the research process—an arena for much needed innovation and leadership from research

funding organizations, research performing organizations (including universities) and the wider plant science community.

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PM and MH jointly planned and wrote the paper. PM took the lead on Sections 1, 2, 5, and 6. MH took the lead on Sections 3 and 4.

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REFERENCES

Altieri, M. (1995). *Agroecology: The Scientific Basis of Alternative Agriculture*. Boulder, CO: West View Press.

Altieri, M. (2002). Agroecology: The science of natural resource management for poor farmers in marginal environments. *Agriculture, Ecosystems and Environment*, *93*(1-3), 1–24. https://doi.org/10.1016/S0167-8809(02)00085-3

Arora, S., van Dyck, B., & Wakeford, T. (2019). Choreographed consensus: The stifling of dissent at CRISPRcon 2019. *The STEPS Centre Blog*, 28.06.2019. Retrieved from https://steps-centre.org/blog/choreographed-consensus-the-stifling-of-dissent-at-crisprcon-2019/

Barben, D., Fisher, E., Selin, C., & Guston, D. (2008). Anticipatory governance of nanotechnology: Foresight, engagement, and integration. In E. Hackett, M. Lynch, & J. Wajcman (Eds.), *The handbook of science and technology studies*, 3rd ed. (pp. 979–1000). Cambridge, MA: MIT Press.

Bioteknologirådet. (2009). Sustainability, benefit to the community and ethics in the assessment of genetically modified organisms. Retrieved from www.bion.no/larkiv/2010/07/2009_11_18_diskusjonsnotat_baerekraft_engelsk.pdf

Bioteknologirådet. (2011). Insektresistente Genmodifiserte Planter og Bærekraft [Insect-resistant genetically modifed plants and sustainability]. Retrieved from http://tema.miljodirektoratet.no/Global/dokumenter/Publikasjoner/Rapporter/rapport_baerekraft_110627_BION.pdf.

Bioteknologirådet. (2014). Herbicide-resistant Genetically Modified Plants and Sustainability. Retrieved from www.bioteknologiradet.no/filarkiv/2014/09/Herbicide-resistant_genetically_modified_plants_and_sustainability_NBAB.pdf.

Bioteknologirådet. (2018). The Gene Technology Act – Invitation to Public Debate. Retrieved from http://www.bioteknologiradet.no/filarkiv/2010/07/genteknologiloven-engelsk-hele-for-web-v-2.pdf

Boenink, M., Swierstra, T., & Stemerding, D. (2010). Anticipating the interaction between technology and morality: A scenario study of experimenting with humans in bionanotechnology. *Studies in Ethics, Law, and Technology*, *4*(2), https://doi.org/10.2202/1941-6008.1098

Borup, M., Brown, N., Konrad, K., & van Lente, H. (2006). The sociology of expectations in science and technology. *Technology Analysis and Strategic Management*, *18*(3–4), 285–298. https://doi.org/10.1080/09537320600777002

Braatz, J., Harloff, H. J., Mascher, M., Stein, N., Himmelbach, A., & Jung, C. (2017). CRISPR-Cas9 targeted mutagenesis leads to simultaneous modification of different homoeologous gene copies in polyploid oilseed rape (*Brassica napus*). *Plant Physiology*, *174*(2), 935–942.

Brown, N. (2003). Hope against hype—accountability in biopasts, presents and futures. *Science Studies*, *16*(1), 3–21.

Brown, N., & Michael, M. (2003). A sociology of expectations: Retrospecting prospects and prospecting retrospects. *Technology Analysis and Strategic Management*, *15*(1), 3–18.

Brown, N., B. Rappert, & A. Webster (Eds.) (2000). *Contested Futures: A Sociology of Prospective TechnoScience*. Aldershot, UK: Ashgate.

Busch, L. (2010). *Standards: Recipes for Reality*. Cambridge MA: MIT Press.

Buttel, F. (2005). The environmental and post-environmental politics of genetically modified crops and foods. *Environmental Politics*, *14*(3), 309–323. https://doi.org/10.1080/09644010500151602

Callon, M., Lascoumes, P., & Barthe, Y. (2009). *Acting in an uncertain world: An essay on technical democracy*. Cambridge, MA: MIT Press.

Carro-Ripalda, S., Astier, M., & Artía, P. (2015). An analysis of the GM crop debate in Mexico. In P. Macnaghten, & S. Carro-Ripalda (Eds.), *Governing agricultural sustainability: Global lessons from GM crops* (pp. 33–73). London: Routledge.

Chilvers, J., Pallett, H., & Hargreaves, T. (2015). *Rethinking energy participation as relational and systemic*. London: UKERC.

CJEU. (2018) Judgment of the Court (Grand Chamber) in case C-528/16, 25 July 2018. Retrieved from http://curia.europa.eu/juris/document/document.jsf?text=&docid=204387&pageIndex=0&doclang=en&mode=req&dir=&occ=first&part=1&cid=584259.

Conway, G. (1999). *The doubly green revolution: Food for all in the twenty-first century*. New York: Cornell University Press.

Dolgin, E. (2017). CRISPR hacks enable pinpoint repairs to genome. *Nature*, *550*, 439–440. https://doi.org/10.1038/550439a

Eckerstorfer, M., Dolezel, M., Heissenberger, A., Miklau, M., Reichenbecher, W., … Waßmann, F. (2019). An EU perspective on biosafety considerations for plants developed by genome editing and other new genetic modification techniques (nGMs). *Frontiers in Bioengineering and Biotechnology*, *7*, 31.

Eckerstorfer, M., Engelhard, M., Heissenberger, A., Simon, S., & Teichmann, H. (2019). Plants developed by new genetic modification techniques—comparison of existing regulatory frameworks in the EU and Non-EU Countries. *Frontiers in Bioengineering and Biotechnology*, *7*, 26. https://doi.org/10.3389/fbioe.2019.00026

Egorova, Y., Raina, R., & Mantuong, K. (2015). An analysis of the GM crop debate in India. In P. Macnaghten, & S. Carro-Ripalda (Eds.), *Governing agricultural sustainability: Global lessons from GM crops* (pp. 105–135). London: Routledge.

ENSSER. (2017). Statement on New Genetic Modification Techniques. Products of new genetic modification techniques should be strictly regulated as GMOs. Retrieved from https://ensser.org/topics/increasing-public-information/ngmt-statement

ESRC (Economic and Social Research Council). (1999). *The Politics of GM food: Risk, Science and Trust*. Swindon: ESRC.

European Commission. (2013). Fact sheet: Science with and for Society in Horizon 2020. Retrieved from https://ec.europa.eu/programmes/horizon2020/sites/horizon2020/files/FactSheet_Science_with_and_for_Society.pdf

Fisher, E., Mahajan, R., & Mitcham, C. (2006). Midstream modulation of technology: Governance from within. *Bulletin of Science, Technology and Society*, *26*(6), 485–496. https://doi.org/10.1177/0270467606295402

Fortun, M. (2001). Mediated speculations in the genomics futures markets. *New Genetics and Society*, *20*(2), 139–156. https://doi.org/10.1080/14636770124557

Fortun, M. (2005). For an ethics of promising, or: A few kind words about James Watson. *New Genetics and Society*, *24*(2), 157–174. https://doi.org/10.1080/14636770500184792

Frewer, L., Lassen, J., Kettlitz, B., Scholderer, J., Beekman, V., & Berdal, K. (2004). Societal aspects of genetically modified foods. *Food and*

Chemical Toxicology, *42*(7), 1181–1193. https://doi.org/10.1016/j.fct.2004.02.002

Friedrichs, S., Takasu, Y., Kearns, P., Dagallier, B., Oshima, R., Schofield, J., & Moreddu, C. (2019). An overview of regulatory approaches to genome editing in agriculture. Conference Report. *Biotechnology Research and Innovation*, *3*(2), 208–220. https://doi.org/10.1016/j.biori.2019.07.001

Fu, Y., Foden, J., Khayter, C., Maeder, M., Reyon, D., Joung, K., & Sander, J. (2013). High-frequency off-target mutagenesis induced by CRISPR-Cas nucleases in human cells. *Nature Biotechnology*, *31*, 822–826. https://doi.org/10.1038/nbt.2623

Fujimura, J. (2003). Future imaginaries: Genome scientists as socio-cultural entrepreneurs. In A. Goodman, D. Heath, & S. Lindee (Eds.), *Genetic nature/culture: anthropology and science beyond the two-culture divide* (pp. 176–199). Berkeley, CA: University of California Press.

Gaskell, G., Allum, N., Wagner, W., Kronberger, N., Torgersen, H., Hampel, J., & Bardes, J. (2004). GM foods and the misperception of risk perception. *Risk Analysis*, *24*(1), 185–194. https://doi.org/10.1111/j.0272-4332.2004.00421.x

Godfray, H., Beddington, J., Crute, I., Haddad, L., Lawrence, D., … Toulmin, C. (2010). Food security: The challenge of feeding 9 billion people. *Science*, *327*(5967), 812–818.

Godfray, H., & Garnett, T. (2014). Food security and sustainable intensification. *Philosophical Transactions of the Royal Society B*, *369*, 20120273. https://doi.org/10.1098/rstb.2012.0273

Goodin, R., & Dryzek, J. (2006). Deliberative impacts: The macro-political uptake of mini-publics. *Politics and Society*, *34*(2), 219–244. https://doi.org/10.1177/0032329206288152

Grove-White, R. (2001). New wine, old bottles: Personal reflections on the new biotechnology commissions. *The Political Quarterly*, *72*(4), 466–472. https://doi.org/10.1111/1467-923X.00426

Grove-White, R., Macnaghten, P., Mayer, S., & Wynne, B. (1997). *Uncertain World: GMOs, Food and Public Attitudes in Britain*. Lancaster: CSEC and Unilever.

Guivant, J., & Macnaghten, P. (2015). An analysis of the GM crop debate in Brazil. I. In P. Macnaghten, & S. Carro-Ripalda (Eds.), *Governing agricultural sustainability: Global lessons from GM crops* (pp. 74–107). London: Routledge.

Gupta, A., & Falkner, R. (2006). The influence of the Cartagena Protocol on biosafety: Comparing Mexico, China and South Africa. *Global Environmental Politics*, *6*(4), 23–55. https://doi.org/10.1162/glep.2006.6.4.23

Guston, D. (2014). Understanding 'anticipatory governance'. *Social Studies of Science*, *44*(2), 218–242. https://doi.org/10.1177/0306312713508669

Guston, D., & Sarewitz, D. (2002). Real-time technology assessment. *Technology in Society*, *24*(1–2), 93–109.

Habets, M., Hove, L., & van Est, R. (2019). *Genome editing in plants and crops: Towards a modern biotechnology policy focused on differences in risks and broader considerations*. The Hague: Rathenau Instituut.

Harvey, P. (2015). An anthropological perspective on the promise and threat of GM Crops. In P. Macnaghten, & S. Carro-Ripalda (Eds.), *Governing agricultural sustainability: Global lessons from GM crops* (pp. 174–178). London: Routledge.

Hedgecoe, A., & Martin, P. (2003). The drugs don't work: Expectations and the shaping of pharmacogenetics. *Social Studies of Science*, *33*(3), 327–364. https://doi.org/10.1177/03063127030333002

Helliwell, R., Hartley, S., Pearce, W., & O'Neill, L. (2017). Why are NGOs sceptical of genome editing? *EMBO Reports*, *18*, 2090–2093.

IFOAM Organics International. (2016). Genetic engineering and genetically modified organisms. Position Paper. Retrieved from https://www.ifoam.bio/sites/default/files/position_genetic_engineering_and_gmos.pdf

IFOAM Organics International. (2017). Compatibility of breeding techniques in organic systems. Position Paper, Retrieved from https://www.ifoam.bio/sites/default/files/position_paper_v01_web_0.pdf

Jasanoff, S. (1995). Product, process or programme: Three cultures and the regulation of biotechnology. In M. Bauer (Ed.), *Resistance to new technology* (pp. 311–332). Cambridge: Cambridge University Press.

Jasanoff, S. (2000). Commentary: Between risk and precaution—reassessing the future of GM crops. *Journal of Risk Research*, *3*(3), 277–282. https://doi.org/10.1080/13669870050043161

Jasanoff, S. (2006). Biotechnology and empire: The global power of seeds and science. *Osiris*, *21*(1), 273–292.

Kearnes, M., Grove-White, R., Macnaghten, P., Wilsdon, J., & Wynne, B. (2006). From Bio to Nano: Learning the lessons, interrogating the comparison. *Science as Culture*, *15*(4), 291–307.

Kosicki, M., Tomberg, K., & Bradley, A. (2018). Repair of double-strand breaks induced by CRISPR–Cas9 leads to large deletions and complex rearrangements. *Nature Biotechnology*, *36*(8), 765–771. https://doi.org/10.1038/nbt.4192

Kusch, S., & Panstruga, R. (2017). mlo-based resistance: An apparently universal 'weapon' to defeat powdery mildew disease. *Molecular Plant-Microbe Interactions*, *30*(3), 179–189.

Kuzma, J. (2019). Biotechnology oversight gets an early make-over by Trump's White House and USDA: Part 2 – The USDA-APHIS Rule. Genetic Engineering and Society Center, NC State, 02 July 2019. Retrieved from https://research.ncsu.edu/ges/2019/07/ag-biotech-oversight-makeover-part-2-usda-aphis-rule/

Ladics, G. S., Bartholomaeus, A., Bregitzer, P., Doerrer, N. G., Gray, A., Holzhauser, T., … Glenn, K. (2015). Genetic basis and detection of unintended effects in genetically modified crop plants. *Transgenic Research*, *24*, 587–603. https://doi.org/10.1007/s11248-015-9867-7

Latham, J., Wilson, A., & Steinbrecher, R. (2006). The mutational consequences of plant transformation. *Journal of Biomedicine and Biotechnology*, *2006*, 25376. https://doi.org/10.1155/JBB/2006/25376

Lawrence, T., & Sudderby, R. (2006). Institutions and institutional work. In S. Clegg, C. Hardy, T. Lawrence, & W. Nord (Eds.), *Sage handbook of organization studies*, 2nd ed. (pp. 215–254). London: Sage.

Lipton, M. (2001). Reviving global poverty reduction: What role for genetically modified plants. *Journal of International Development*, *13*(7), 823–846.

Ludwig, D., & Macnaghten, P. (2020). Traditional ecological knowledge in innovation governance: a framework for responsible and just innovation. *Journal of Responsible Innovation*, *7*(1), 26–44. https://doi.org/10.1080/23299460.2019.1676686

Lund Declaration. (2009). The Lund Declaration: Europe must focus on the grand challenges of our time. Swedish EU Presidency, 8 July, Lund, Sweden.

Macnaghten, P. (2016). Responsible innovation and the reshaping of existing technological trajectories: The hard case of GM crops. *Journal of Responsible Innovation*, *3*(3), 282–289.

Macnaghten, P., & S. Carro-Ripalda (Eds.) (2015). *Governing agricultural sustainability: Global lessons from GM crops*. London: Routledge.

Macnaghten, P., & Owen, R. (2011). Good governance for geoengineering. *Nature*, *479*, 293.

Mallapaty, S. (2019). Australian gene-editing rules adopt 'middle ground'. *Nature*, https://doi.org/10.1038/d41586-019-01282-8

Marris, C., Wynne, B., Simmons, P., & Weldon, S. (2001). *Public perceptions of agricultural biotechnologies in Europe*. Final Report of the PABE Research Project commissioned by the European Commission Centre for the Study of Environmental Change, Lancaster. Retrieved from http://csec.lancs.ac.uk/archive/pabe/docs/pabe_finalrepot.pdf

Marx, V. (2014). Gene editing: How to stay on-target with CRISPR. *Nature Methods*, *11*(10), 1021–1025. https://doi.org/10.1038/nmeth.3108

Mehrotra, S., & Goyal, V. (2012). Agrobacterium-mediated gene transfer in plants and biosafety considerations. *Applied Biochemistry and Biotechnology*, *168*, 1953–1975. https://doi.org/10.1007/s12010-012-9910-6

Michalopoulos, S. (2018). Industry shocked by EU Court decision to put gene editing technique under GM law. Euractiv.com. Retrieved from https://www.euractiv.com/section/agriculture-food/news/industry-shocked-by-eu-court-decision-to-put-gene-editing-technique-under-gm-law/

Ministry of Health, Labour and Welfare. (2019). *Food hygiene handling procedures for food and additives derived from genome editing technology*. Government of Japan: Retrieved from https://www.mhlw.go.jp/content/000550824.pdf

Ministry of the Environment. (2018). *To genome editing technologies users*. Government of Japan: Retrieved from https://www.env.go.jp/press/2_2_%20genome%20editing_En.pdf

Montenegro de Wit, M. (2020). Democratizing CRISPR? Stories, practices, and politics of science and governance on the agricultural gene editing frontier. *Elementa: Science of the Anthropocene*, *8*(1), 9. https://doi.org/10.1525/elementa.405

Murphy, J., & Levidow, L. (2006). *Governing the transatlantic conflict over agricultural biotechnology: contending coalitions, trade liberalisation and standard setting*. London: Routledge.

Nap, J., Metz, P., Escaler, M., & Conner, A. (2003). The release of genetically modified crops into the environment. Part I. Overview of current status and regulations. *The Plant Journal*, *33*(1), 1–18.

National Research Council. (1989). *Field testing genetically modified organisms – Framework for decisions*. Washington DC: National Academy Press.

Newell, P., & Glover, D. (2003). *Business and Biotechnology: Regulation and the Politics of Influence*. Institute of Development Studies Working Paper 192. Brighton, UK: University of Sussex.

Norris, A., Lee, S., Greenlees, K., Tadesse, D., Miller, M., & Lombardi, H. (2020). Template plasmid integration in germline genome-edited cattle. *Nature Biotechnology*, *38*(2), 163–164. https://doi.org/10.1038/s41587-019-0394-6

Northcott, M. (2015). Crop Science, the heisenberg principle and resistance to genetically modified crops. In P. Macnaghten, & S. Carro-Ripalda (Eds.), *Governing agricultural sustainability: Global lessons from GM crops* (pp. 198–204). London: Routledge.

Nuffield Council on Bioethics. (2012). *Emerging biotechnologies: technology, choice and the public good*. London: Nuffield Council on Bioethics.

OpenPlant. (2020). OpenPlant Synthetic Biology Research Centre. Retrieved from https://www.openplant.org/

Owen, R., Macnaghten, P., & Stilgoe, J. (2012). Responsible research and innovation: From science in society to science for society, with society. *Science and Public Policy*, *39*(6), 751–760. https://doi.org/10.1093/scipol/scs093

Peng, R., Lin, G., & Li, J. (2015). Potential pitfalls of CRISPR/Cas9-mediated genome editing. *FEBS Journal*, *283*(7), 1218–1231. https://doi.org/10.1111/febs.13586

Pielke, R. (2007). *The honest broker: Making sense of science in policy and politics*. Cambridge: Cambridge University Press.

Plantum. (2019). Plantum-visie genome editing. Plantum. Retrieved from https://assets.plantum.nl/p/229377//files/Plantum-visie%20genome%20editing.pdf.

Pretty, J., Sutherland, W. J., Ashby, J., Auburn, J., Baulcombe, D., Bell, M., … Pilgrim, S. (2010). The top 100 questions of importance to the future of global agriculture. *International Journal of Agricultural Sustainability*, *8*(4), 219–236. https://doi.org/10.3763/ijas.2010.0534

Raina, R. (2015). Institutional rigidities and impediments: Agricultural research and GM crops in India. In P. Macnaghten, & S. Carro-Ripalda (Eds.), *Governing agricultural sustainability: Global lessons from GM crops* (pp. 212–219). London: Routledge.

Rommens, C. (2018). Pandora's Potatoes: The Worst GMOs. CreateSpace Independent Publishing Platform.

Royal Society. (2009). *Reaping the benefits: Science and the sustainable intensification of global agriculture*. London: The Royal Society.

Schuurbiers, D. (2011). What happens in the lab: Applying mid-stream modulation to enhance critical reflection in the laboratory. *Science and Engineering Ethics*, *17*(4), 769–788.

Selin, C. (2007). Expectations and the emergence of nanotechnology. *Science, Technology and Human Values*, *32*(2), 196–220.

Stilgoe, J., Owen, R., & Macnaghten, P. (2013). Developing a framework of responsible innovation. *Research Policy*, *42*(9), 1568–1580.

Stoate, C., Boatman, N., Borralho, R., Rio Cavalho, C., de Snoo, R., & Eden, P. (2001). Ecological impacts of arable intensification in Europe. *Journal of Environmental Management*, *63*(4), 337–365. https://doi.org/10.1006/jema.2001.0473

Stone, G. (2017). Dreading CRISPR: GMOs, honest brokers and Mertonian transgressions. *Geographical Review*, *107*(4), 584–591. https://doi.org/10.1111/gere.12260

Sustainable Pulse. (2020). Scientist warns UK Government: scrapping the EU's strict GMO rules would threaten health. Retrieved from https://sustainablepulse.com/2020/02/06/scientist-warns-scrapping-the-eus-strict-gmo-rules-threatens-health/?utm_source=newsletter&utm_medium=email&utm_campaign=glyphosate_gmos_and_pesticides_weekly_global_news_bulletin&utm_term=2020-02-10#.Xk__BJNKg6h

Sykes, K., & Macnaghten, P. (2013). Opening up dialogue and debate. In R. Owen, J. Bessant, & M. Heitz (Eds.), *Responsible Innovation: Managing the responsible emergence of science and innovation in society* (pp. 85–107). Chichester: John Wiley.

Tan, L., Li, X., Liu, F., Sun, X., Li, C., Zhu, Z., … Sun, C. (2008). Control of a key transition from prostrate to erect growth in rice domestication. *Natural Genetics*, *40*(11), 1360–1364. https://doi.org/10.1038/ng.197

USDA. (1986). How the federal government regulates biotech plants. USDA: Retrieved from https://www.usda.gov/topics/biotechnology/how-federal-government-regulates-biotech-plants

USDA. (2018). Secretary Perdue issues USDA statement on plant breeding innovation. USDA Press Release Release No. 0070.18, 28.03.2018. Retrieved from https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation

van den Hoven, J., P. Vermaas, & I. van de Poel (Eds.) (2015). *Handbook of ethics, values, and technological design: Sources, theory, values and application domains*. Cham: Springer.

Vats, S., Kumawat, S., Kumar, V., Patil, G. B., Joshi, T., Sonah, H., … Deshmukh, R. (2019). Genome editing in plants: Exploration of technological advancements and challenges. *Cells*, *8*(11), 1386. https://doi.org/10.3390/cells8111386

von Schomberg, R. (2013). A vision of responsible research and innovation. In R. Owen, J. Bessant, & M. Heintz (Eds.), *Responsible innovation: Managing the responsible emergence of science and innovation in society* (pp. 51–74). London: Wiley.

Wickson, F., & Wynne, B. (2012). The anglerfish deception. *EMBO Reports*, *13*(2), 100–105. https://doi.org/10.1038/embor.2011.254

Williams, L., & Macnaghten, P. (2019). Whose deficit anyway? Institutional misunderstanding of fracking sceptical publics. In E. Turnout, W. Tuinstra, & W. Halffman (Eds.), *Environmental expertise: Connecting science, policy and society* (pp. 90–103). Cambridge University Press: Cambridge.

Williams, L., Macnaghten, P., Davies, R., & Curtis, S. (2017). Framing fracking: Exploring public responses to hydraulic fracturing in the UK. *Public Understanding of Science*, *26*(1), 89–104.

Wilsdon, J., & Willis, R. (2004). *See-through-science: Why public engagement needs to move upstream*. London: Demos.

Wynne, B. (2001). Creating public alienation: Expert cultures of risk and ethics on GMOs. *Science as Culture*, *2*(4), 321–337. https://doi.org/10.1080/09505430120093586

Wynne, B. (2006). Public engagement as a means of restoring public trust in science: Hitting the notes, but missing the music? *Community Genetics*, *9*(3), 211–220. https://doi.org/10.1159/000092659

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