Overcoming Obstacles to Gene-Edited Solutions to Climate Challenges

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Gene editing and genetic modification hold enormous potential to deliver solutions to multiple climate change challenges. The most important rate-limiting obstacles impeding their development and deployment are not technical, but rather counterproductive policies and regulations. These are driven in part by the mistaken apprehension of widespread public opposition. These obstacles are described and solutions to overcoming them are presented.

Jared Diamond observed that,

> Any society goes through social movements or fads, in which economically useless things become valued or useful things devalued temporarily. Nowadays, when almost all societies on Earth are connected to each other, we cannot imagine a fad's going so far that an important technology would actually be discarded. A society that temporarily turned against a powerful technology would continue to see it being used by neighboring societies and would have the opportunity to reacquire it by diffusion (or would be conquered by neighbors if it failed to do so).
>
> —Diamond (1997)

Crops improved through biotechnology, often called genetically modified organisms (GMOs),[1] have made major contributions to improved agricultural productivity and sustainability, increasing farmer incomes, improving environmental health, food safety, and benefitting consumers worldwide (Klümper and Qaim 2014; Nicolia et al. 2014; ISAAA 2020; Brookes 2022a,b). Gene editing has already accelerated the rate at which such benefits are being imagined, developed, and delivered and holds the potential to help rapidly address some of the critical challenges associated with reducing greenhouse gas (GHG) emissions, as others have shown (Asanuma and Ozaki 2020; DeLisi et al. 2020; Giddings et al. 2020; Ito 2021; Houser 2022; Rosenzweig 2022; Zahoor 2022). Yet, despite these considerable benefits and the urgent need for these solutions, opposition and obstacles threaten to delay or block such beneficial applications. This paper describes the most important obstacles and shows how they can be overcome.

RATE-LIMITING FACTORS

Other papers have described several gene-edited innovations that hold significant promise for reducing GHG emissions and/or drawing down atmospheric levels of carbon dioxide. Technical

[1]Some have tried to draw a distinction between "genetic engineering" by which they mean the use of recombinant DNA techniques to insert exogenous DNA into a genome, and "gene editing" defined as limited to tweaking extant DNA sequences in a genome. But as technology advances, gene-editing techniques are increasingly being used to achieve similar or identical results as genetic engineering (Irving 2022; Yarnall et al. 2022) so we use the terms as more or less synonymous.

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obstacles remain to be conquered before these and other related innovations can be reduced to practice and deployed at scale but the promise for sizable and rapid impacts is high. The primary rate-limiting factor is not technical challenges, but regulatory and policy burdens based on the perception of problems with public acceptance (Lee 2022).

Public acceptance is difficult to measure. Opinion surveys of widely differing quality have delivered varying results over the past four decades. The common wisdom suggests there is considerable public hesitation, if not downright resistance, at least to foods improved through biotechnology. But while there are some regions in which this may be true—e.g., Austria—the reality is more complicated (Keller 2021), and the data tell a very different story.

There is often a gap, sometimes dramatic, between what people self-report about their attitudes in a public opinion survey, and their attitudes as manifest in actions. People often say one thing and do another. Indeed, it has been known for decades that many people simultaneously hold mutually contradictory views, particularly when it comes to genetic technologies (Office of Technology Assessment [OTA] United States Congress 1987). This is particularly so with regard to survey responses versus point-of-purchase decisions on whether or not to buy a product. But consumer data from around the world show consumers consistently base food purchase decisions on three factors: cost, taste, and quality. This holds true even among populations where a significant number claims otherwise (International Food Information Council [IFIC] 1921; Office of Technology Assessment [OTA] United States Congress 1987).

The reality is that every bushel of genetically engineered corn or soy that has been grown has been sold, and the market has not delivered a consistent premium for non-genetically engineered varieties. (Some soy varieties have consistently commanded premium prices for specialty varieties such as those used for tofu; but the market size for such varieties is too small to support the regulatory costs for approval of genetically modified [GM] varieties at present) (McDougall 2011; Lassoued et al. 2019; Whelan et al. 2020).

The agronomic and commercial success of crops improved through biotechnology has led directly to the explosive adoption of biotechnology-improved seed by farmers around the world (ISAAA 2020). This holds true not only for countries where biotech-improved seeds have been approved by governments, but also where farmers have been denied access by governments that have been slow to recognize the reality of their safety and superior sustainability (Giddings 2019). But the mistaken perception of broad consumer reluctance has been both a cause and effect of policies and practices that needlessly discriminate against biotechnology innovations in agriculture.

The result is policies, regulations, and business practices such as "non-GMO" certification, all of which create disincentives and barriers to the development and deployment of innovative solutions developed with gene editing and genetic engineering. This is the case around the world despite the lack of scientific justification for such discrimination, and in the face of massive experience demonstrating the superior safety and sustainability of such technologies (Smyth 2022).

The barriers created by these regulations, policies, and practices must be overcome if products of gene editing/genetic engineering are to be developed and deployed in a timely manner.

WHAT IS TO BE DONE? 1—REDUCING REGULATORY BURDENS

There is no doubt that well-designed regulations have contributed to enormous societal benefits by improving the safety of foods, devices, and tools, and reducing the unintended negative consequences of innovations (Havens 1978; Guasch and Hahn 1999; O'Toole 2014). But regulations that are not well designed and impose compliance burdens disproportionate to the benefits they aspire to deliver are counterproductive, and not "fit for purpose."

In the name of safety, regulatory regimes around the world impose burdens on the introduction and use in food and agriculture of innovations developed through biotechnology. These burdens are disproportionate to the actual hazards the innovations embody. The sanitary and

phytosanitary (SPS) agreement of the World Trade Organization (WTO), and the International Plant Protection Convention (IPPC) codify standards that safety regulations must meet to ensure regulations actually advance safety rather than provide a cover for surreptitious goals, such as protectionism. Distilled to their essence, these standards stipulate that regulatory measures must address an actual threat (i.e., exposure to an identified hazard), not a hypothetical fear; they must be proportional to that threat; and they must not be excessive, more restrictive than necessary to manage or mitigate the threat. These standards form the foundation of the rules-based system of international trade in food commodities, on which food security for much of the world depends. But regulations applied to crops and foods improved through biotechnology around the world fall short of complying with these standards.

Governments generally take one or the other of two different approaches to safety assurance for crops and foods improved through biotechnology: one aims to ground regulations and approval decisions in data and build on experience; the other, despite claiming otherwise, elevates other criteria, such as "precaution" or political concerns. The United States, Australia, Canada, Japan, Argentina, Brazil, and some others fall into the first category, although not perfectly. The European Union and countries that follow the EU example, particularly in tropical latitudes, fall into the latter category.

The United States first promulgated a major biotechnology policy statement in 1986, publishing an approach to regulation known as the Coordinated Framework (CF) (Office of Science and Technology Policy [OSTP] Executive Office of the President 1986). The CF is based on the recognition that no novel risks of GMOs have been identified (i.e., no potential for exposure to novel hazards) compared to those familiar with crops and foods developed with traditional methods of genetic improvement (e.g., classical breeding, wide crosses, tissue culture) (National Academy of Sciences 1987, 1989; Kuiper et al. 2001; European Commission 2010). The OSTP, therefore, posited that existing legislation assigning authority to manage and mitigate such familiar hazards to avoid unreasonable risks should be adequate to the task. Public comment was solicited and received confirming these facts. Regulatory agencies within the U.S. Department of Agriculture, Animal and Plant Health Inspection Service (USDA), Environmental Protection Agency (EPA), and Food and Drug Administration (FDA) were tasked with developing regulations, as necessary, to implement the CF, which they did in accord with their own authorities.

The FDA determined that existing methods for ensuring food safety were sufficient—sellers are responsible for the safety of the food they sell, and if a food had a history of safe consumption, it would avoid major premarket regulatory scrutiny. If the food was novel in some potentially hazardous way and lacked a history of safe use, the FDA laid out a consultation mechanism in which the agency asked questions to test the basis for a seller's claim of its safety.

The EPA developed a series of policies to confirm the safety of new pesticidal substances developed through biotechnology, but the USDA was the first agency to promulgate new regulations to deal with "GMOs." In accordance with the standards laid out in the CF, the U.S. Department of Agriculture, Animal and Plant Health Inspection Service (USDA) (1987) defined the regulatory trigger capturing "GMOs" for review according to the characteristics of the product—whether or not it presented a potential plant pest risk. This was established by the presence or absence of DNA sequences from a listed plant pest—the mere use of recombinant DNA technologies is/was insufficient to trigger regulatory oversight. Experience soon showed this criterion was not, in fact, a reliable marker for hazard (National Academy of Sciences 1989, 2000, 2002; Organization for Economic Cooperation and Development [OECD] 1992, 1993), and the Animal and Plant Health Inspection Service (APHIS) revised its application of the trigger to narrow the scope of items captured for premarket review and streamline the process (U.S. Department of Agriculture, Animal and Plant Health Inspection Service [USDA] 1992).

According to the CF, this approach of gaining experience with classes of new products (e.g.,

herbicide-tolerant maize, insect-resistant cotton, confirming safety, and reducing regulatory burdens while refocusing attention on areas of remaining uncertainty) should have become a regular pattern. Despite some encouraging moves in recent years, this has not happened (U.S. Department of Agriculture 2018). And over the past four decades, all U.S. regulatory agencies have drifted from the path envisioned in the CF, although none have wandered farther than the FDA. In its most recent proposals to ensure the safety of plants and animals improved through gene editing, the FDA has adopted a "guilty until proven innocent" approach that flies in the face of reason and experience (Van Eenennaam and Young 2014; Giddings 2017a,b). Not only is this approach not what is required under the law, but it is also scientifically nonsensical (Van Eenennaam et al. 2019; Van Eenennaam 2022).

As bad as the situation has been in the United States, it is far worse elsewhere in the world. The European Union adopted a "precautionary approach" that presumes biotech-improved seeds present novel hazards and unreasonable risks despite the absence of supporting data or experience (European Commission 1990; Paarlberg 2001; Entine 2006). The EU instituted a process so burdensome and political as to block nearly all farmer adoption of seeds improved through biotechnology and causing the world leading seed innovation industry, once found in Europe, largely to relocate to the United States (Torry 2012). Innovation in European agriculture has thus lagged behind the rest of the industrial world, as has also been the case for other countries that have followed the European example (ISAAA 2020).

The global situation today is that in virtually every jurisdiction, the disharmony between the degree of regulatory scrutiny applied to biotechnology-derived innovations in food and agriculture, and the level that would be proportional to the actual hazards and risks, has grown from a gap to a chasm. This degree of regulatory scrutiny does nothing to add to citizen safety, and such regulations are not "fit for purpose" (United Kingdom Advisory Committee on Releases to the Environment [UKACRE] 2013a,b,c; Gould et al. 2022). They serve only to prolong reliance on older, if not obsolete, technologies, the products of which are generally less safe and less efficient than more recent innovations.

This means that the use of the most advanced seed-improvement technologies, with a remarkable record of safety and improvements in sustainability and productivity, are disincentivized and discriminated against despite such policies being contradicted by vast amounts of data and experience. Inasmuch as genomes throughout nature are salted with sequences imported from other lineages (Ridley 1999; Giddings 2015) to the extent that everything that appears on a dinner plate throughout most of the world is naturally transgenic, the irony is palpable. This represents a massive failure of policies in countries around the world that is especially egregious in the face of present challenges and needs. The opportunity costs of such retrograde policies are considerable (Gouse et al. 2016; McFadden et al. 2021; Usla 2022; Paarlberg and Smyth 2023).

The solution is as simple as it is obvious: regulations lacking justification in data and experience must be set aside as rapidly as possible. Detailed accounts of how this can/should be accomplished are not lacking (United Kingdom Advisory Committee on Releases to the Environment [UKACRE] 2013a,b,c; European Academies Science Advisory Council [EASAC] 2013; Conko et al. 2016; Giddings 2017a, 2021, 2022; Eriksson 2018; Gould et al. 2022). Their recommendations should be taken up and acted upon as a matter of urgency in the United States, Europe, and other countries around the world.

WHAT IS TO BE DONE? 2—ELIMINATING MISLEADING AND FRAUDULENT LABELS

Unduly burdensome regulations and innovation-hostile policies are the major impediments to the development and deployment of biotechnology-derived solutions to climate change problems and other societal challenges. But other forces also play an inimical role, including ill-founded labeling requirements or standards.

Some governments, particularly those in the European Union and its emulators, under the rubric of informing consumers, have mandated

labels on foods containing "GMO"-derived ingredients above a certain threshold. The criteria triggering the EU "GMO" labeling requirements use the following language (European Commission 1997):

- Foods and food ingredients containing or consisting of GM organisms within the meaning of Directive 90/220/EEC;
- Foods and food ingredients producted [sic] from, but not containing, genetically modified organisms.

The definition of "GMO" found in Directive 90/220 is "genetically modified organism (GMO) means an organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination" (European Commission 1990).

The problems with this approach are manifold. First, the triggering content threshold of 0.9% is purely arbitrary, and bears no relationship to any meaningful measure of health, safety, nutrition, quality, etc. Second, the class of foods and food ingredients captured for labeling contains multiple exceptions, also arbitrary and unrelated to any meaningful criterion related to health, safety, nutrition, or otherwise (European Parliament 2003). And finally, and fatally, the definition of GMO as "an organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination" is purely nonsensical. Every "genetic modification" made in the production of any GMO or gene-edited product is made with enzymes scientists first found in nature; they are used to effect the same kinds of genetic changes observed widely throughout nature. Examples of discovery of gene transfer found in nature that are directly analogous, if not entirely indistinguishable from genetic modifications effected by scientists using naturally occurring enzymes to effect naturally occurring mechanisms of genetic change in the laboratory, are abundant (Wang et al. 2006; Schneider and Thomas 2014; Yong 2014, 2017; Gasmi et al. 2015; Jones 2015; Kyndt et al. 2015; Matveeva and Otten 2019; Chen et al. 2022). Far from defining any meaningful class, this definition of "GMO" does little more than signal the biological illiteracy of those who conjured it (Johnson 2015; Tagliabue 2015, 2016, 2020; Wood 2022). Together with requirements for traceability, labeling, and testing, the European Union has constructed a compliance nightmare for which there is no shred of scientific justification, in gross violation of its obligations and responsibilities under the SPS/WTO and the IPPC (World Trade Organization 1994; IPPC 1997).

The argument that consumers want and have a "right to know" is equally unsound. Consumers fed a steady diet of propaganda and lies for years by vested interests (Academics Review 2014; Wetaya 2022b) without meaningful pushback from the governments supposedly safeguarding their interests will, of course, say they want labels to tell them whether or not they are buying GMOs, even though nobody can give them a definition of GMO that is not nonsense. But experience shows consumers reliably respond in the affirmative whenever they are asked if they want to have information on a label or otherwise available, because they are rightly skeptical of those who would propose to withhold meaningful information (Hackleman 1981). But when presented with a blank slate asking them what information they want on a label, very few indicate they want information on "GMOs." Consumer demand for GMO labels, in this case, is an artifact of inept opinion polls and ongoing propaganda campaigns by vested interests (Academics Review 2014; English 2019; Food Insight 2021; Lynas et al. 2022).

Perhaps the most egregiously false and misleading GMO label is not mandated by the government, but results from a business plan that appears to be based on fomenting unfounded fears about competing products and misleading consumers. The Non-GMO Project, a company created by a coalition of organic marketers will, for a fee, license the use of their label (a butterfly logo) to deceive consumers through false and misleading claims about foods, food ingredients, and their health and safety characteristics (Savage 2016; Giddings and Atkinson 2018; Miller 2018). Their marketing uses the label as a symbol to reassure consumers that a product is

free of GMOs, even though they admit on their own website that it in fact provides no such guarantee. Such misleading labels defy both FDA and Canadian guidance on the topic and are in clear violation of the law (Campbell 2018; English 2019; FDA 2019; Canadian General Standards Board 2021). Such propaganda campaigns from vested interests contribute to the demonization of safe, more sustainable products and valuable technologies. Tolerating them imposes significant societal costs (Gelski 2016; English 2022).

WHAT IS TO BE DONE? 3—ACCELERATING PUBLIC ACCEPTANCE IS THE ESSENTIAL PREREQUISITE

Improving the acceptance climate among policymakers and regulators is essential if solutions developed through genetic engineering and gene editing are to be deployed. Many different actions can help improve the acceptance climate, from increased participation by scientists and informed citizens in science communication and policymaking, to sustained programs by credible independent entities including NGOs and think tanks.

Pushing back against the concerted disinformation campaigns from special interests that have driven such discriminatory policies is difficult, particularly for governments, but independent, science-based voices are well suited for the task. There are several entities with proven track records in this space, and publications from several are cited in the references below:

- The Genetic Literacy Project (GLP): https://geneticliteracyproject.org;
- The Institute for Food and Agricultural Literacy (IFAL): https://ifal.ucdavis.edu;
- The International Service for the Acquisition of Agri-Biotech Applications (ISAAA): https://www.isaaa.org/kc/default.asp;
- PG Economics: https://pgeconomics.co.uk/publications; and the
- Information Technology and Innovation Foundation (ITIF): https://itif.org/issues/agricultural-biotech.

These groups are critically important contributors to enabling future innovations built on genetic technologies.

There are reasons to be hopeful that these obstacles to gene-edited and genetically engineered solutions will be overcome (Baksi 2022; Bayer 2022; Bounds and Terazono 2022). As noted above, the existing regulatory regimes have been harshly criticized, particularly in recent years. And decades of empty alarms of health and environmental calamities from the use of GMOs have corroded the credibility of opposition groups (Brown 2022; Gelski 2022), even as some of them have changed course (Morgan 2021; RePlanet 2022). Governments, particularly those in developing countries, have noticed the considerable benefits delivered by crops improved through biotechnology and are moving to avail themselves of the same rewards (Awal 2022; Das 2022; Maina 2022; Mong'ina 2022; NatureNews 2022; Wetaya 2022a; Zongo 2022). The perception of consumer opposition also seems to be declining (Food Insight 2021; Baksi 2022; Bayer 2022). But the need for climate change solutions these technologies can deliver is urgent, and it would be imprudent to rely on the natural corrections Diamond (1997) identified to remove the remaining obstacles (Bayer 2022; Doudna 2022; The Economist 2022). Philanthropic support for the independent advocates identified above can make a critical impact and provide a rapid return on investment. Such support should be provided as rapidly as possible. The risks of action need to be compared not to a presumed no-risk-if-we-don't-act path, but to the very real, well understood, scientifically grounded, and truly dire risks of staying the current course.

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