Deficits of Public Deliberation in U.S. Oversight for Gene-Edited Organisms

By Jennifer Kuzma

Innovation pathways for emerging technologies like gene editing present few opportunities for public deliberation and engagement, yet scholars continue to call for public inclusion in decision making to enhance procedural democracy and legitimacy, as well as the quality of outputs. One public window occurs during federal rulemaking and major regulatory actions. Here, public comments are solicited through the Federal Register. However, this mode suffers serious limitations—low level of public representation, narrow scope of valid input, and unidirectional communication. For example, public comments must address narrow technical regulatory authorities in order to be considered. The reality is that regulatory assessments and decision processes for biotechnology products are most often closed to a handful of federal agency staff and product developers. Thus, the preferences of technological experts and biotechnology developers dominate product reviews, resulting in bias towards technological optimism and product approval. The release of gene-edited organisms (GEdOs) into complicated socio-ecosystems are made under conditions of high uncertainty with limited evidence to support long-term ecological or human safety. Yet in some cases, their impacts on ecosystems may be irreversible. For unconfined environmental releases of novel GEdOs and gene-drive organisms (GDOs), this "democratic deficit" may ultimately put ecosystems and public health in jeopardy, as unconflicted experts and skeptical stakeholders are excluded from decision-making and unavailable to critically examine potential risks and benefits. Scientific objectivity suffers with no one to question technical or social assumptions and provide alternative scenarios for the future under these ambiguous conditions. This essay reviews the need for and challenges to opening-up regulatory processes for GEdOs and GDOs to outside experts, stakeholders, and publics. Public deliberation will be required to elicit independent technical advice, draw on experiential wisdom in areas of proposed GEdO and GDO release, ameliorate dangers of technological optimism, and increase the legitimacy of release decisions.

Gene Editing and Gene Drives

Genetic engineers can now precisely cut and delete particular sites of DNA, replace portions of genes, or add entirely new genes in specific places through gene editing. Gene editing is akin to our abilities to take pen to paper to correct typos, delete words or phrases, rearrange sentences, or add new ones. CRISPR Cas9 is a gene-editing system that can be guided more specifically to any site in the DNA by its accompanying RNA sequences (called "guide RNA" or gRNA). After the CRISPR-Cas 9 system (with the gRNA) cuts the target DNA site, a double-strand break results that can either be successfully repaired by the cell or result in a mutation. However, if engineers provide a DNA template sequence with homology to either side of the break at its ends, it can be used for repair instead and copied into the break site, causing a larger edit or deletion in that gene, or the introduction of a new gene depending on how the template is designed. Furthermore, if the repair templates also include DNA sequences of CRISPR-Cas and the gRNA (aka the CRISPR-Cas 9 system), then CRISPR-Cas9 system can copy itself into cleavage sites via homology directed repair. If these constructs are incorporated into germ-line cells the system will be inherited at a super-Mendelian rate and is called a "gene drive."

Gene drives rely on gene editing but take it a step further in order to spread genes through wild populations. Usually, an introduced gene is carried on one of a pair of chromosomes and is thus inherited by about half of the offspring in the first generation. Eventually the gene will get diluted in the natural population if there is no selective advantage to it. However, "gene-drive" systems allow for an edited gene on one chromosome to copy itself into its partner chromosome. The result is that nearly all offspring will inherit the engineered gene. The idea is that even if just a few organisms with gene drives are released into the wild, the whole population could end up with the edited gene.

To achieve the desired effect on populations, the gene-drive system can be engineered to cut a sex-linked gene (e.g., lethal to females at the larval stage) so that the drive causes the population to decline (only males survive). Alternatively, a drive system can be engineered to carry extra "cargo" genes into populations to confer desirable traits, like disease resistance. If the gene drive is linked to an engineered genetic allele of interest, it can result in that allele being inherited by almost 100% of the offspring. This drives the gene into each successive generation until the

entire population contains it. Theoretically, cargo genes can come from any species and be introduced into any host.

Several reasons to use gene drives to engineer populations in the wild have been proposed. For example, they could spread killer-genes to destroy unwanted pest populations, invasive species, or disease-carrying organisms. The release of just a few individuals with gene-drive systems that are designed to kill organisms could theoretically cause the whole population to collapse. This could come in handy for eradicating mosquitos carrying Dengue, malaria, or Zika virus or for eliminating invasive species like mice that threaten endangered birds on islands. In contrast, gene drives could also be used to add beneficial genes to populations. Editing systems like CRISPR-Cas9 could carry cargo genes with them to immunize an endangered species against disease or protect it from the effects of climate change. Ecological risks and benefits of gene-drive organisms (GDOs) are difficult to predict and could cause permanent changes to ecosystems. The potency and permanency of certain gene drives underscore the importance of making publicly robust and inclusive decisions prior to release. However, innovation, regulatory, and decision-making systems in the United States are not currently equipped to include stakeholder and public engagement or deliberation as described below.

Innovation Systems: No place for public deliberation

Federal funding and grants are the starting point for innovation in the United States, as they support academics and small companies to develop the basic and applied science that underpins gene-editing product development. Patents and licensing agreements help to transfer discoveries out of the public sector and into larger companies who then perfect the technologies and their applications for the market. Gene-edited products would not have been possible without public investments stemming from citizens and residents who pay taxes. For example, the National Institutes of Health, a taxpayer-funded government research agency, invested over $3 billion dollars in CRISPR research from 2011 to 2018.[1] However, there is not a venue for the public to have input into areas of investment for federal R&D or choices about which applications of gene-editing should or should not be developed.

To date, GM crops and gene-edited crops have largely been targeted at meeting food processor and farmer needs.[2] In contrast GDOs have been developed for public health and conservation purposes with foundation investments, like in the case of Target Malaria funded by the Gates

Foundation. Either way, despite their role in underwriting gene-editing technology, the U.S. public has little input into which applications get developed and presented to regulatory agencies. Power and control are largely in the hands of biotech developers and their funders from discovery through product development and until regulatory decision-making.

Regulatory Systems—a Window for Public Input?

The Administrative Procedures Act (APA) requires some public transparency and input in federal agency regulations and rules. All major, proposed regulatory actions must be published in the Federal Register and undergo a period of public comment. The APA mandates that agencies publish a Notice of Proposed Rulemaking (NPRM) in the Federal Register to allow interested parties affected by the rule to submit written data, views, or arguments. The process takes place in three stages: a pre-proposal stage (Advanced Notice of Proposed Rule Making), a second stage which involves a public comment or public hearing period (NPRM), and finally, public notice of the final rule. Federal oversight for biotechnology products is the first formal place where public input in innovation decisions is sometimes sought. However, this process is imperfect at best, as described below. First, a brief description of the regulatory system for biotechnology products is provided, followed by a look at where the formal oversight system for biotech products falls short with regard to public engagement.

Regulation for U.S. Biotechnology Products

The U.S. Coordinated Framework for the Regulation of Biotechnology (CFRB) guides federal oversight for biotechnology products like GEdOs and GDOs. Stemming back to its origins in 1986, the CFRB is based on the premises that 1) the risks of biotech products are the "same in kind" as conventional products; 2) the product should be the focus of regulation, not the process by which it is made; and, 3) therefore, no new laws were needed to oversee biotechnology products. Existing laws and product categories were used to divide regulatory responsibilities among three key federal agencies. Sometimes the fit between emerging biotechnology products and older, existing laws has been tenuous under the CFRB, and authorities been interpreted loosely and have changed over time. For example, recently the jurisdiction for genetically engineered (GE) mosquitos toggled from the Food and Drug Administration (FDA) to a split between FDA and the Environmental Protection Agency (EPA) depending on the claim of use by the developer—that is whether the GE mosquito is used to mitigate disease or for general pest control.[3] In 2021, contemporary struggles for jurisdiction for GE animals under various laws are

taking place between the U.S. Department of Agriculture (USDA) and FDA.[4] Furthermore, the risk-based premises of the Coordinated Framework have been challenged, particularly by several consumer and environmental non-governmental organizations, who claim that risks can be tied to certain "processes" of genetic engineering like the use of antibiotic markers, off-target gene edits, and gene expression systems that are not under natural control. Regardless, the Coordinated Framework remains in place today for overseeing emerging products of genetic engineering like GEdOs and GDOs.

Under the Coordinated Framework, the USDA has regulated genetically engineered (GE) plants as "plant pests" under the Federal Plant Pest Act (of 1957) (revised as the Plant Protection Act in 2000). USDA passed regulations in 1987 for field trials and in 1993 for interstate movement (called "deregulation") of GE plants. Early in the days of plant biotechnology, GE plants were made by using engineered sequences from the plant-pest, Agrobacterium, in order to deliver genes into plants and to express them. Thus, the DNA fragments from plant-pests provided a regulatory hook for the USDA, even if the gene of interest for a desired trait had nothing to do with a plant pest. However, in the past few decades, plant biotechnologists started engineering plants without the use of plant-pest DNA sequences or by removing them from the final product. In 2010, USDA decided to exempt GE plants without plant-pest DNA sequences from its regulatory authorities under the "Am I Regulated" letter inquiry process. Over 100 GE plants from 2010 to 2020 were exempted from USDA's pre-market regulation.[5] Many of these were gene-edited crops. Then, in 2020, USDA passed revisions to its regulations for GE plants which focus on "plant-pest" risk issues rather than presence or absence of plant-pest DNA. However, USDA continues to exempt several categories of gene-edited crops from pre-market regulation.[6] Plant biotech developers can decide that their product is exempt under these categories and introduce it into the market without submitting any information to regulatory agencies or in the public domain.[7] Furthermore, new labeling laws for bioengineered foods exempt food products that do not have foreign DNA in the final product and thus exclude gene-edited foods from mandatory labeling.[8] In summary, the current regulatory system allows for the introduction of certain gene-edited crops into agricultural, environmental and food systems without regulation or public disclosure.

EPA has also interpreted its authorities under the CFRB to regulate GE plants and microbes. GE plants engineered with pesticidal-like proteins are regulated under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as pesticides (plant-incorporated protectants), and GE microorganisms are regulated as "toxic chemicals" under Toxic Substances and Control Act (TSCA). Recently EPA proposed to treat gene-edited plants as exempt under its FIFRA regulations for plant-incorporated protectants, as long as the edited or introduced DNA can be found in sexually compatible species.[9]

For food safety review under the Coordinated Framework, the FDA developed a voluntary consultation policy based on the concept of "substantial equivalence." As a category, GE food products are seen as substantially equivalent to conventionally bred food products; therefore, the FDA does not require a mandatory regulatory process for GE foods. In 1992, the FDA published guidance for this voluntary consultation process under the Federal Food Drug and Cosmetic Act (FDCA), asking GE developers to consult with the agency about the safety of their plant-based GE foods. To this day, the FDA's process does not involve a formal determination of safety. The agency reviews data voluntarily submitted by GE-food companies and then writes a letter indicating that the agency has no safety concerns about the product at that time.

In 2009, the FDA also put forth a policy exerting authority for GE animals under the New Animal Drug Act, with the claim that the gene is like a drug as it affects the physiology of the animal. However, as mentioned above, USDA recently proposed to transfer authority for GE animals from FDA to USDA if the GE animal is one involved in food production. USDA proposes to use a variety of existing laws for regulating GE animals, such as the Animal Health Protection Act.

The National Environmental Policy Act (NEPA) also has a role across all three agencies of the Coordinated Framework. It requires that all federal agencies follow established environmental review procedures, which include evaluating and documenting the environmental impact of any significant federal action. Regulations under NEPA establish three levels of environmental review with progressively greater detail and rigor: categorical exclusions, environmental assessments (EA), or environmental impact statements (EIS). Agencies can use lower level of environmental review, the EA process, if the decision is not a major federal action predicted to

significantly affect the quality of the human environment. If the decision is considered to have major potential impacts, the EIS process must be utilized.

Although NEPA is a procedural statute and not technically used to approve or deny a biotech product, it is place where public participation is mandated and applies to all decisions about the release of GEdOs and GDOs that are regulated under the Coordinated Framework. NEPA requires open public meetings if a full-blown EIS is selected as the review pathway. However, the vast majority of decisions on genetically modified organisms (GMOs) have not gone through this process but through the less-involved EA and Finding of No Significant Input (FONSI) process.

Compliance with NEPA has been a point of contention in the regulation of GMOs. For example, lawsuits have been brought against the USDA by consumer, organic, and environmental groups on the grounds that GE plants were not adequately assessed by USDA because the agency did not choose to draft an EIS. Some of these cases have been won in federal courts.[10] The first-ever EIS was conducted on a GE crop in 2010 as a result of one of these federal cases, although GE crops have been released into agroecosystems since 1987 and on the open market since 1995. Several consumer and environmental groups have also sued the FDA for its approval of the GE AquaAdvantage Salmon, and one reason for the lawsuit was the lack of a full EIS.[11]

Public Input into Regulatory Decision-Making

As described above, GEdOs released into agricultural or environmental systems may not require any U.S. regulation and therefore, no public input would need to be solicited through the comment-and-rulemaking or EIS process. Plant biotechnologists are increasingly turning to gene-editing not only for the technical advantages, but also because many gene-edited crops will likely not be regulated.[12] Even if some gene-edited plants are captured under the new 2020 USDA regulations (i.e., those not automatically exempt), they are unlikely to undergo risk assessments or EIS processes, and there will be no requirements for public input or disclosure of their entry into the market.[13]

In contrast, gene-drive animals, such as mosquitos and mice for pest-eradication, may require some regulation by the FDA as a "new animal drug" or by the EPA as a "biopesticide." Therefore, in theory, some public input would be obtained through the APA's notice-and-public comment in rulemaking and perhaps through NEPA's EIS procedures. However, oversight

systems are not trending in this direction. For example, in summer 2020, the EPA approved the first open field-releases of a GE mosquito strain (OX 5304) not only without conducting an EIS but also without publishing the risk assessment prior to the APA's mandated public-comment period. OX5304 is a precursor technology to GDOs, as the GE mosquito contains a female-killing system designed to drive down the *Aedes aegypti* population which carrying dengue and Zika viruses. The EPA granted the experimental use permit which allows for open releases of OX 5304 across FL and TX without any scientific advisory committee process, with no published and peer-reviewed studies on OX5304 available for independent scientific scrutiny, and without publishing the risk assessment in the Federal Register docket for public comment prior to the decision being made.[14] For such a landmark decision—the first open-scale release of a GE insect that acts like a gene drive in the wild (i.e. its genes will spread and drive down the population)—the lack of public input into the decision and oversight process is striking. Furthermore, at the local level, the FL Keys Mosquito Control Board heard only from Oxitec, the maker of OX5304, in formal presentations at its board meetings. Although public members were able to comment for a few minutes at a time, no independent scientists or stakeholders were invited to present to the board before it approved the partnership with Oxitec to help deploy their OX5304 mosquitos in the Florida Keys over summer 2021.

In the case of OX5304, scientific information and the risk assessment was not available prior to the comment period or a decision being made. However, even if a GEdO or GDO is regulated and a draft assessment is available for comment in the Federal Register prior to decision-making, there is consensus in the social science and policy literature that public comment in rulemaking is a poor form of public participation.[15] It is a process that few people know exists, and comments must be directed at the narrow authorities under consideration. For example, GDOs for disease control may be reviewed under FDA's new animal drug authorities, and the main criteria for "animal drug" approval are safety to the animal and efficacy of the drug. If public comments during rulemaking pertain to general public health or ecological safety of GDOs, technically, the agency need not consider these comments. It also does not have to consider any value-based concerns like socioeconomic or cultural impacts. Finally, notice-and-comment in rulemaking is a unidirectional form of public engagement, which is not ideal under any conditions for increasing the quality of the decision or legitimacy.

In summary, innovation systems for GDOs and GEdOs remain largely closed to the public, and regulatory systems only briefly open in the Federal Register should the products come under federal oversight. Still this mode of public inclusion is inadequate to foster legitimacy and trust in GDO and GEdOs release, as well as to ensure scientific rigor and independent scrutiny.

Without Public Deliberation, Risk Assessments Suffer

In recent years, federal agencies have not sought external peer-review or convened advisory comments for key decisions about genetically engineered organisms. For example, the very first genetically modified insect was approved for release by FDA in 2016 with no advisory committee or peer-review of the risk assessment. Then EPA in 2020 approved another version of this GM insect, OX5304, with no independent advisory committee process and without publishing the risk assessment prior to the public comment period. Around 2011, the first gene-edited plant was deemed by USDA not to require regulation without any external, public process. These major decisions about emerging biotechnology products were made behind closed doors by product developers consulting with agency officials. This is problematic, as product developers have a financial stake. Conflicts of interest are also prevalent with many federal agency staff members who weave in and out of the biotech industry.[16] Agency staff are also under significant pressure from Congress to decrease regulatory burdens for biotech products.[17] It has been shown that government risk evaluations can be biased towards approving GMOs under conditions of uncertainty.[18]

For GDOs, even more will be at stake if risk assessments and regulatory review are biased. GDOs raise new and magnified challenges for risk governance in comparison to the deployment of other genetic engineering technologies. Gene drives are meant to spread through a wild population; whereas regulation of GMOs has typically been based on containment or confinement in managed settings (e.g., agriculture), especially for field trial stages.[19] Oversight systems designed for GMOs are unlikely to be sufficient for GDOs for these reasons, and greater precaution may be warranted.[20] The goal of spread also presents challenges to field monitoring and testing, forcing wide boundaries and more resources for data collection. The escape of even one GDO from a limited field trial could in some cases (depending on gene-drive design) spread a gene throughout an entire population. Impacts on ecosystems are hard to predict, and GDO

impacts could be irreversible. Conducting risk assessments to ensure that they are "strongly objective"[21]—with the participation of multiple experts, stakeholders, and interested and affect parties—will be crucial for ensuring GDO safety.

Risk analysis is laden with assumptions and interpretations based on values. For example, the endpoints we choose to evaluate in a risk assessment are based on what we care about (e.g., certain species, certain natural resources, certain human illnesses). Also, uncertainty in risk analysis leads to various interpretations of the data to which we bring our own experiences, cultures, and worldviews. Even in relatively straightforward cases of chemical risk assessment, the choice of a mathematical-model for generating a dose-response curve from laboratory studies is an endeavor in which one can be more or less precautious about estimating risk under release conditions. Even if we do have good information on the dose-response curve, the level at which something is presumed "safe" is debatable as safety is a socially defined concept. Science gives us a guide, but what risks are acceptable is based on values, taking into consideration our experiences, culture, perceptions of the benefits, control over the situation, and trust in those managing the risks. Even agency regulatory assessments of biotechnology products conducted by experts show unwarranted bias toward product approval, making inaccurate textual claims with the goal to minimize claims about risk.[22]

GDOs present a case for risk analysis where data and information are severely limited, and therefore values will play even more of a prominent role in decision-making. Quantification of risk in advance of any field releases will be nearly impossible given the uncertainties associated with GDOs in complex socio-ecological systems and the stochasticity of movements of organisms across geographic boundaries or rare genetic transfer events. GDOs have features of "emerging risks" that are "characterized mainly by uncertainty regarding their potential consequences and/or probabilities of occurrence" which "can be due to a lack of knowledge about causal or functional relationships between new risk sources and their environment or to the insufficient application of available knowledge to the case in question."[23] For these situations, evaluating the "substantive validity" of risk assessments—where outcomes of the risk assessment are compared to what happens in reality—is not feasible, especially prior to any environmental release. Therefore, "procedural validity" of the risk assessment, that is *how* the

risk assessment is conducted, becomes even more important than attempting to ascertain the substantive validity of particular risk evaluations prior to GDO release and field data collection.

Deliberation Frameworks for Risk Analysis & Governance

Post-normal science (PNS)[24] suggests that when the decision stakes are high and the system uncertainties great, extended peer and stakeholder communities (beyond scientific researchers) should be consulted to interpret what is known and what it means for the policy decision at hand. Diverse values become an explicit part of risk assessment as the "facts" are uncertain and require interpretation for their meaning. People with "on-the-ground" knowledge, who are "interested and affected,"[25] are invited into the deliberations about risk and safety measures, along with a broader range of scholars such as ethicists and social scientists. Scientific experts and government managers still provide important technical analysis, but democratic engagement opens up the policy process for characterizing risk to communities in areas of potential GDO deployment, giving them not only a voice but also a choice in deciding what levels of risk are acceptable to them.

Another framework for conducting risk analysis in support of formal regulatory decision-making, the "Procedurally Robust Risk Analysis Framework" (PPRAF) has been proposed that draws upon principles of humility, procedural validity, inclusion, anticipation, and reflexivity.[26] Particular considerations for regulatory risk analysis under PPRAF are to 1) assess social and behavioral foundations of vulnerability to risk, 2) consider distributive impacts of risks amongst different groups, 3) promote mutual learning as object of deliberation in risk analysis, 4) engage multiple interested and affected parties in discussion of ends and means of innovation, 5) elicit the input of interested and affected parties for scoping the risk problem and at key junctures in risk assessment, 6) examine assumptions and framing in risk analysis, 7) acknowledge alternative explanation to the data and analysis, 8) reflect on quality of organizational processes used for risk analysis, 9) reflect on meaning of any potential errors to outcomes, 10) assess the quality of the process that led to the risk estimation, 11) proceed with openness and transparency in conduct of risk analysis, 12) ensure consistency in interpretation of data and information, 13) account for changing future conditions at different timescales, and 14) consider contingencies of what is known, plausible, possible, and unknown for the future.

Barriers & Incremental Change for Deliberation

Barriers to public deliberation are deeply embedded in political and regulatory structures, as well as the minds of people inhabiting different sectors in technological innovation systems. Biotechnology innovators (and sometimes regulators) hold the power for what gets researched and put into the marketplace. Their predominant bias is that biotechnology is needed to save us from ever-decreasing food supplies, environmental destruction, and economic peril under conditions of population growth and climate change. The national political conversation often focuses on biotechnology remaining unimpeded by regulation to maintain U.S. competitiveness and job growth.[27] Skeptics and critics, even when well-informed, are marginalized if they hold alternative perspectives on the place of biotechnology in society. Many biotech advocates dismiss critics as un-scientific or "luddites", regardless of their credentials. Biotechnology advocates often subscribe to the "deficit model"[28]—that is, people generally do not understand the science behind biotechnology and therefore, they cannot form valid viewpoints to inform decision-making.

In our studies on attitudes towards responsible research and innovation (RRI), we have found a divide in how biotech product-developers view what it means to responsibly innovate in comparison to scientists and well-versed stakeholders from consumer and environmental groups.[29] Social science scholarship largely identifies four pillars of RRI—anticipation, inclusion, responsiveness, and reflexivity.[30] Anticipation entails asking the 'what if. . .?' questions. The aim is to take into consideration contingencies, what is known, what is likely, what is plausible and what is possible under a variety of future scenarios and changing environmental, social, or cultural conditions. Inclusiveness involves engaging diverse public voices in discussions about the ends and the means of innovation. Reflexivity requires that technology developers and societies examine their own activities and assumptions to gain an awareness of the limits of their knowledge and framing biases. Responsiveness involves the capacity to change the shape or direction of innovation in response to stakeholder and public values and circumstances.

We found that biotech developers are less supportive of RRI principles of public inclusion and responsiveness than anticipation and reflexivity.[31] They worry about relinquishing control as it may stifle innovation and slow down R&D in hyper-competitive funding and financing climates.

If publics are invited into conversations and decisions about biotech products, biotech developers and advocates are also afraid that people will fear GEdOs and GDOs—called in previous literature, "biotechphobia-phobia"[32]—and these public scares will slow down biotechnology innovation. We also found that federal government agency representatives, while more supportive of public inclusion and responsiveness, are hampered by the narrow legal authorities under which they operate (e.g. "plant pest" of USDA or "new animal drugs" for FDA) which do not support public deliberation or broader input in regulatory assessments beyond the Federal Register rulemaking process.

In light of these and other barriers, policies to formally integrate public inclusion and responsiveness in federal biotech product decisions are needed. Piecemeal authorities for biotech products under the Coordinated Framework might preclude a holistic look at risks, benefits, societal impacts, and ethical dimensions if public deliberation is conducted under just one federal agency. Supra-agency structures that go beyond individual agencies and legal authorities for biotech products might better accommodate the diverse viewpoints and concerns that should be considered during public engagement and deliberation. The National Academies of Science Engineering and Medicine (NASEM) suggested a one-stop shop for oversight of emerging biotech products that would tailor the level of public deliberation to the novelty and complexity of the product.[33] GDOs are highly novel with complex ecosystem interactions, and under the NASEM model, they would require public deliberation in conjunction with external expert review, such as through federal advisory committees, and agency assessments. The one-stop shop suggested by the NASEM could be the Office of Science and Technology Policy, if it could maintain public trust and project a more neutral stance on biotechnology innovation. Better yet, OSTP could contract with a third-party, independent organization to conduct public deliberation and external peer-review.

Gene-edited plants might present fewer and less complex interactions in agroecosystems when compared to GDOs. Under the NASEM model, they would seem to require public input, along with expert external review, but perhaps not as deep and sustained public deliberation as required for GDO releases. However, gene-edited crops are already entering the food system without any mandatory regulation or labeling, and consumers remain largely unaware of their existence. For most gene edited foods, there will be no greater food safety risks in comparison to conventional

crops or 1st generation GM foods, but the lack of pre-market oversight to ensure substantial equivalence and environmental safety is troublesome. In the absence of formal oversight structures, gene-edited crop developers should take the helm to engage publics and experts in their voluntary assessments, perhaps through a third-party neutral moderator.[34] Advocacy groups should continue to pressure these companies to do so.

As it stands now, the process for regulatory assessment of GMOs, and now GDOs and GEdOs, is woefully lacking in scientific rigor, external peer review, and public input. Conflicted biotech enthusiasts hold the most power in decision-making spaces, and there is evidence that this leads to biased regulatory assessments upon which release decisions are predicated.[35] Greater public involvement in GDO and GEdOs oversight will be required in order to improve the rigor and legitimacy of risk assessments.

However, expectations for executing bidirectional and wide-scale public deliberation for every GDO or GEdO should be managed. Resources are limited, delays to biotech innovation could be unwarranted, and pushback from biotech developers and advocates would be significant. Adoption of a model like the NASEM suggests, where greater levels of public inclusion and deliberation are evoked depending on the complexity and novelty of the biotech product, seems more realistic. It would also make sense to have a rigorous external, advisory committee review tied to public deliberation and input for the first biotech product in a category of products—for example, the first gene-edited insect proposed for environmental release, the first gene-edited animal in human food systems, or the first gene-edited plant with a certain trait. Certainly, such a process should be in place for the first GDO release.

However, as reviewed herein, significant barriers exist for broader inclusion of outside experts, stakeholders and publics. Technology developers are reticent to relinquish their existing control, given pressures of global scientific competition, paradigms of techno-economic growth, and limited sources of project financing. Federal agency staff are limited in engaging stakeholders and publics by current administrative procedures and legal authorities. Skeptics and critics of biotechnology will need to open their minds to engage meaningfully with biotech developers as well. Broader inclusion and deliberation for meaningful public input into regulatory assessments and decisions about GDOs and GEdOs will remain a pipedream without significant policy change mandating its existence, institutional redesigns, and attitudinal shifts in biotech skeptics

and advocates. These aspirations would enable regulatory institutions and biotech innovation systems not only to benefit from the insights, collaboration, and experiential wisdom of interested and affected publics, but also to demonstrate their legitimacy and trustworthiness.

Notes

[1] Congressional Research Service. *Advanced Gene Editing: CRISPR-Cas9* (2018). https://crsreports.congress.gov/product/pdf/R/R44824/6

[2]USDA. Am I regulated? https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated/. This USDA site keeps a record of gene-edited crops presented to USDA for regulatory jurisdiction decisions from 2010-2020. On this site, gene-edited crops have traits mainly for better food processing qualities or farming practices. Very few address consumer needs, and when they do, there is another motivation such as for food processing (e.g. high oleic acid soybean, non-browning lettuce).

[3] FDA. Clarification of FDA and EPA Jurisdiction Over Mosquito-Related Products Guidance for Industry #236 (2017). Available at https://www.fda.gov/media/102158/download. If the developer makes a *disease mitigation* claim for a GM mosquito that drives down the mosquito population that carries a virus like Dengue, it would be overseen by FDA. If the developer does not make that claim, but rather a general *pest control* claim, it would be overseen by EPA. Oxitec was able to shift authorities for its GE *Aedes aegypti* products between FDA and EPA after 2017 by downplaying disease mitigation claims.

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[13] J. Kuzma & K. Grieger, "Community-Led Responsible Governance."

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[15]C.R. Farina, M. Newhart, and J. Heidt. "Rulemaking vs. democracy: Judging and nudging public participation that counts." *Mich. J. Envtl. & Admin. L.* 2 (2012): 123.

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