A Framework for

RESPONSIBLE USE OF GENE EDITING IN AGRICULTURE

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COALITION FOR
RESPONSIBLE
GENE EDITING
IN AGRICULTURE

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A FRAMEWORK FOR RESPONSIBLE USE OF GENE EDITING IN AGRICULTURE

Introduction

Gene editing is one of many different methods that scientists, breeders and farmers use to create improved varieties of plants, animals, microbes and other organisms. By making targeted changes in DNA, scientists are able to turn a gene's expression on or off and recreate a gene from within the species' family. Gene editing's highly targeted approach can bring about improvements in a single generation of plant or animal, while previous breeding methods were far less precise and could take generations to be effective.

In recent years, new gene editing techniques have accelerated its potential to benefit society and agriculture. This evolution of advanced breeding technology can reduce agriculture's environmental impact, contribute to sustainable agricultural practices, provide important advancements for farming in the developing world, improve nutrition and food quality for consumers, improve animal welfare, increase disease resistance for plants and animals, enhance productivity for farmers around the world and address challenges faced by agriculture due to climate change.

However, it is well recognized that gaining social license to develop and commercialize products derived from the technology is necessary for gene editing's full potential to be realized. Consumers today are demanding safe, healthy food produced in a socially responsible manner, and they are demanding greater transparency. It is in this consumer-centric environment that gene editing technology is being brought to market. For gene editing in agriculture to deliver on its full promise, the products of gene editing must be accepted and supported by the food system and ultimately by consumers.

This framework is intended to increase transparency and stakeholder engagement to build trust in the products derived through gene editing and those using them.

About the Framework

This framework has been developed by representatives from food companies, academic institutions, farmer organizations, non-governmental organizations, gene editing product developers and related associations. The Center for Food Integrity was guided in its development by a multi-stakeholder Steering Committee that is responsible for the content of this document. A list of Steering Committee members can be found at geneediting.foodintegrity.org. *Participation on the Steering Committee does not imply endorsement of the framework by the individuals or their respective organization.*

The Framework is overseen on an ongoing basis by the Framework Oversight Committee. Oversight includes regular review of framework content, soliciting input from users and stakeholders, and final authority for approval of framework content.

The Framework Oversight Committee is comprised of a cross-section of framework users and stakeholders with an interest in gene editing and includes developers, representatives of civil society, product buyers and users, and academics as detailed in the coalition governance document.

About the Coalition

The Coalition for Responsible Gene Editing in Agriculture was formed by The Center for Food Integrity to create a framework that supports acceptance of gene editing technology in agriculture and food. Coalition participants share the goal of earning trust in gene editing.

A Coalition Operations Committee provides resources and direction for all initiatives of the CFI Coalition for Responsible Gene Editing in Agriculture. Leadership includes representatives from technology developers, food companies, farmers and related associations in addition to advisors from universities, civil society and other institutions that bring expertise and diverse perspective on societal expectations. Visit geneediting.foodintegrity.org for a full committee roster. *Participation in Coalition committees does not imply endorsement of the framework by the individuals or their respective organization.*

Objectives

The goal of the Coalition is to provide a framework for responsible use that provides assurance to the food system and other stakeholders that those using gene editing within the framework do so in the best interests of agriculture, the food system and society in general.

To achieve its goal, the framework must be credible, workable and affordable. The framework is designed to provide adequate transparency and appropriate oversight to be accepted as credible by a broad range of stakeholders. The framework must also be workable and affordable for the wide range of entities that use gene editing, including researchers and commercial enterprises of varying sizes.

SCOPE AND APPLICATION

Definition of Gene Editing

Gene editing encompasses a suite of technologies designed to intentionally alter predetermined DNA sequences in the genome and result in precise, targeted insertions, deletions or other changes for genetic improvement. The Responsible Use of Gene Editing framework was developed with non-transgenic applications in mind.

Scope

The scope of this framework covers organizations developing applications or products using gene editing in food and agriculture. It is intended to apply to any corporation, business, academic or governmental organization that utilizes gene editing and/or its outputs in the commercial research, development or manufacture of food and agricultural products. The intent is to identify and share organizational policies, procedures and practices that demonstrate a commitment to responsible gene editing. These policies and practices may be applied at the product level, but unless specified in the framework, information is to be provided at the organization level.

Those developing the framework are based in the United States with the intent to share the framework for consideration globally. This framework commits organizations utilizing gene editing to comply with all relevant laws, rules, and regulations that may govern plants, animals, microbes and other organisms developed using gene editing technologies in the markets where they have business activities. Those using the framework are committed to operate in ways that facilitate the flow of goods in commerce.

The framework intentionally acknowledges the role regulations play in assuring food safety and protecting the environment and animals, and is not intended to duplicate any existing regulatory framework nor provide any warranty or guarantee of efficacy or safety.

It also encourages and assumes that organizations and individuals involved in gene editing strive to act in accordance with professional, research and ethical standards as recommended by appropriate scientific and professional organizations.

In addition to legal compliance, those following the framework agree to adopt policies and practices consistent with the following principles, and to voluntarily provide assurance of conformance as defined by the Verification section of this framework.

FRAMEWORK PRINCIPLES

The framework is based on principles identified as important in building trust: Transparency, Stakeholder Engagement, Safety and Quality, Trade and Market Considerations, Social Considerations, Continuous Improvement, and Verification.

Principle: Transparency

Assurance of responsible use of gene editing goes beyond simply stating users are being responsible. Access to meaningful, accurate and clear information is a cornerstone of trust.

Organizations seeking to demonstrate responsible use must, within the limits required to protect intellectual property and confidential business information, implement processes for:

- **Meaningful documentation and disclosure of processes used to develop gene-edited products.**
- **Comprehensive and forthright disclosure of the technology used in production to include:**
  - **Disclosing the scientific concepts at work in the gene-edited product in a relatable manner for effective communication with interested stakeholders.**
  - **Communicating in a way that promotes comprehension among a non-specialist audience and avoids confusing terminology.**
- **Commitment to transparent and effective communication of conformance with this framework.**

Organizations using the framework will, within the limits required to protect intellectual property and confidential business information, transparently share information and engage with stakeholders and consumers about the application of gene editing technologies. Information to be shared will include:

- **The nature of gene editing methods employed,**
- **Intended use and benefits of proposed products,**
- **Plausible safety concerns, if any, and how they are being managed,**
- **Mechanisms for stakeholder input and feedback during the life of the product, and**
- **Information that allows the public to know that a gene-edited agricultural product may be part of the food chain, where applicable.**

The need to protect intellectual property and confidential business information may limit transparency at certain stages of the development and commercialization process, but those involved in gene editing should always strive for more transparency rather than less. When there are legitimate reasons for not sharing, those reasons should be disclosed.

Confidential Business Information (CBI): Information that is maintained as confidential by the developer and may relate to trade secrets, processes, operations, style of works or other information of commercial value, the disclosure of which could cause substantial harm to the competitive position of the business or organization.

CBI guidance: The Framework encourages companies to define CBI appropriately and maximize transparency.

Examples of what is likely included: trade secrets (i.e. formulas, recipes, manufacturing processes and marketing strategies), business processes, business operations, inventory details, customers or clients, revenue sources, and cost of goods.

Principle: Stakeholder Engagement

Framework participants will engage a balanced and representative group of stakeholders to anticipate the economic, environmental and social implications, positive or negative, of product development projects, and engage with end users and other relevant stakeholders at an early stage in order to understand their needs and concerns. Organizations will engage in public dialogue and clearly explain what they are doing, why they are doing it, what the potential public benefits are, what the plausible safety concerns, if any, are, and how these are being addressed. They avoid overstatements as to the benefits and safety of their work.

An organization's product development process should provide meaningful and accessible opportunities to offer input and feedback. Stakeholder trust will be based, in part, on the frequency and success of activities in these areas.

Principle: Safety and Quality

Framework participants recognize safety and quality is important to all stakeholders. Organizations following the framework are committed to the ethical, legal and safe use of biological materials. Organisms or products developed using gene editing carry no unique safety concerns or risks vs. organisms developed using other selective breeding techniques. We recognize that to maintain trust, framework participants should disclose steps taken to assure safety and quality and to meet applicable regulatory requirements.

Creating a culture of quality and safety must be a priority for organizations following the framework. Quality management systems assure that applications or products meet the intended performance or quality attributes. Identifying policies, processes, and procedures being utilized provides transparency for product stewardship and quality management.

Framework participants recognize public concerns about potential off-target edits* and unintended consequences as a result. Because of gene editing's precision, the likelihood of unintended changes to the DNA with negative impact is much lower with gene editing as compared to natural genetic variation or products produced using other breeding techniques. Consistent with our commitment to transparency, the Responsible Use framework includes commitments specific to off-target edits to acknowledge the concern and convey appropriate scientific rigor to minimize and mitigate any such occurrences.

Off-target definition:

* *An off-target edit is defined as an unintended change to a DNA sequence that can occur during genome editing due to the sequence similarity between the off-target site and the intended target*

Principle: Trade and Market Considerations

An overarching commitment in the framework is compliance with relevant laws, regulations and standards in the country in which the developer/company operates, as well as in key markets* as identified in a trade and market risk assessment. Due to the global nature of agriculture and food, organizations should have in place policies and practices that support products being developed using gene editing technologies and are managed in a responsible manner that:

- **supports international trade,**
- **facilitates the flow of goods in commerce,**
- **enables choice and coexistence with diverse production systems, and**
- **meets applicable regulatory requirements in key countries of production and import with functioning** regulatory systems.**

Referencing the 2009 BIO launch guide:

* *Meet applicable regulatory requirements in key markets (which at a minimum shall include the United States, Canada, and Japan) prior to commercialization of a new biotechnology product in commodity corn, soybeans, and canola in the United States or Canada, unless determined otherwise in consultation with the value chain for the crop.*

** *A "functioning" regulatory system is science-based, with clearly defined timelines and processes for regulatory review and decision-making, and appropriate protection for proprietary information and data. The regulatory decision-making processes must be predictable, completed in a timely manner, and not subject to undue political influence.*

Principle: Social Considerations

Consumers expect food to be safe and are increasingly interested in how food production systems impact social responsibility, environmental sustainability, food animal welfare and other factors. Acknowledging and addressing potential social considerations is an important step in meeting expectations for transparency and building trust in gene editing.

The aim of the social consideration process is to help individuals and groups engaging with gene editing consider a variety of perspectives on different topics. It is designed to stimulate dialogue and support better-informed decisions that address potential challenges and embrace the opportunities associated with gene editing.

As part of framework participants' commitment to transparency and stakeholder engagement, this is an opportunity to proactively address social considerations and potential impacts, positive or negative, we know are important to stakeholders. This calls for open discussion and sharing of ideas, and a readiness to engage others who bring diverse perspectives to the conversation.

Principle: Continuous Improvement

The Coalition is committed to improving organizational performance and the framework model. The Administrative and Verification Bodies will provide support and training to assist gene editing organizations in effectively utilizing the framework to improve organizational performance. The framework will be reviewed and revised as needed to integrate learning about new technologies, best practices and results of monitoring and evaluation activities. The framework will be reviewed periodically to ensure that its requirements contribute to the Coalition's defined objectives.

Principle: Verification

Framework participants recognize that consumers and other stakeholders may require assurance that they are, in fact, living up to their commitments and following the Responsible Use Framework. Independent verification provides demonstrable evidence that framework participants are meeting the spirit, intent and specifications of the framework. The verification mechanism is designed to be credible, evidence-based, and feasible for a range of organizations in terms of complexity and cost to comply.

COMMITMENTS AND GUIDANCE

For each principle, the framework lists policies or actions that demonstrate participating organizations' commitment to the principle. These commitments vary by stage of product development (see Definitions).

Guidance is provided for each commitment to indicate ways organizations may demonstrate that their actions are consistent with the commitments to the overarching principle. The examples listed in the framework are illustrative only and are not intended to be exhaustive or the only ways to demonstrate conformance. Supporting resources provide additional guidance to help framework participants implement the framework.

Definitions

Gene Editing

Gene editing encompasses a suite of technologies designed to intentionally alter predetermined DNA sequences in the genome and result in precise, targeted insertions, deletions or other changes for genetic improvement.

Off-target Edit

An off-target edit is defined as an unintended change to a DNA sequence that can occur during genome editing due to the sequence similarity of the off-target site and the intended target.

Development Stages

- **Commercial Research**

  Pursuit of advancing scientific knowledge with the intent of commercialization. Includes research to determine possible uses for the findings or to determine new ways of achieving some specific and predetermined objectives. Research includes proof of concept experimentation that is required as part of product development. Commercial research can occur in a company or academic setting.

- **Commercial Development**

  Work using existing knowledge gained from research or practical experience for the purpose of creating new or improved products/processes. For the Coalition's purposes Commercial Research becomes Commercial Development when gene editing is applied to an organism in order to directly achieve a pre-defined commercial product goal. This includes, but is not limited to, licensing, field trials, scale-up production and other pre-commercial activity.

- **Commercial Sales**

  Market introduction and/or sale of products.

- **Product Lifecycle**

  Includes post-introduction monitoring, manufacturing, distribution, issues response and product discontinuation.

A. Transparency Commitments

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
1. Publicly pledge support for/commitment to the framework. **Guidance:** ▪ Framework participants will be publicly listed on the Coalition for Responsible Gene Editing website as supporters of the Responsible Gene Editing Framework and in the process of being verified. Once a participant completes the Verification Process, the organization will be listed on Responsible Gene Editing website as in full conformance with the framework. ▪ Applicants will create and post a statement of support for Coalition values and principles as they apply to their organization.	X	X	X	X
2. Make summary of policies and practices relevant to conformance with framework principles available to interested stakeholders on a publicly available website. **Guidance:** ▪ More detailed information about each policy or practice will be available upon request, subject to confidential business information constraints. ▪ For universities, information may be published on a college, school or department website (vs . a laboratory-specific site) and may include university policies as well as requirements to qualify for government research funding.	X	X	X	X
3. Communicate the advantages and disadvantages of gene editing and the benefits of resulting products or applications. **Guidance:** ▪ When sharing application or product information, the expectation is that it will be at a species/crop/organism and trait combination level. Organizations are not required to share information at the individual hybrid or variety level.		X	X	X

A. Transparency Commitments *(cont.)*

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
4. Proactively seek input from interested stakeholder groups (both supportive and critical) as appropriate based on the stage of the product development process, novelty of application and potential for stakeholder concern or other issues. **Guidance:** ▪ See Stakeholder Engagement section for more specific guidance on Commitments to seek input at each of the development stages.		X	X	X
5. If a regulatory submission needed to enable a commercial release is made to a U.S. regulatory agency for a gene-edited agricultural product, there should be public acknowledgement of the regulatory submission identifying the organism, trait, and the agency to which the submission has been made. This should be done within 45 days of the application being complete. **Guidance:** ▪ Complete is defined as when the regulatory agency determines that it has the information required to complete its assessment ▪ For animals "complete" is when the Administrative New Animal Drug Application has been filed, as that is when all the technical sections are deemed completed, or adequate, under an Investigational New Animal Drug process. ▪ For the two above provisions, confidential business information need not be made available. In addition, if a regulatory agency requires that the applicant keep its submissions confidential, then it should not be disclosed. However, if a regulatory agency is prevented from making the submission public but the applicant is not prevented by law, then the applicant should abide by the two obligations above.		X	X	X
6. At a time no later than the announcement that a product is being commercially released, a summary of the regulatory submission and the non-confidential business information from the underlying regulatory submission shall be made publicly available.				

A. Transparency Commitments *(cont.)*

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
7. For a product of gene editing that is exempt from pre-market regulatory review in the U.S., and a regulatory submission is not made, and is on a commercial track (i.e. commercial candidate lines identified), there should be public acknowledgement of the organism, trait type, and exemption, no later than one year prior to planned commercial introduction. **Guidance**: ▪ For plants, information should be made public not more than 120 days after the developer makes an exemption determination. ▪ Such an acknowledgement should include the basis of the exemption. ▪ Confidential business information is not expected to be made publicly available. ▪ Prior stakeholder engagement might indicate earlier public disclosure would be beneficial. ▪ Information should be posted on a company, trade association or other organization website or online resource.		X	X	X
8. If conducted, provide access on a public website to summaries of research on safety and environmental impact, positive or negative. Provide background data and analysis of summarized studies upon request, subject to confidential business information. **Guidance:** ▪ When sharing application or product information, the expectation is that it will be at a species/crop/organism and trait combination level, not at the individual hybrid or variety level.			X	X
9. Commit to publicly share unanticipated adverse effects revealed after commercialization, if any, (within 60 days of confirmation by agency with jurisdiction) to human or animal health or the environment, and resulting resolution activities. **Guidance:** ▪ Adverse impact and resolution activities should be posted on a company website within 60 days of confirmation by the agency.			X	X
10. Once a microorganism, crop or animal/trait is commercially available, make information available that allows the public to know that it may now be part of the food chain, where applicable. **Guidance:** ▪ Information should be made publicly available through the commercial life of the product vs. a one-time announcement such as a press release. This may be accomplished through a company, trade association or other organization website or online resource.			X	X

B. Stakeholder Engagement Commitments

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
1. Have a stakeholder engagement plan to proactively and reactively engage with stakeholders who express an interest or may potentially be interested in their work. **Guidance:** ▪ Stakeholder engagement plans should be scalable based on stage of development, interest and potential impact, positive or negative, of the product/technology. ▪ Stakeholder engagement plans should include actions that promote effective engagements by: 1) giving voice to stakeholders, 2) acknowledging they have been heard, and 3) explaining how and why decisions have been made. ▪ Stakeholder engagement plans will vary by stage of product development and may include: • Stakeholder mapping to identify appropriate audiences, including/with special attention to marginalized groups or those most likely to be affected positively or negatively by the product/technology • Contact mechanisms such as mail, email, website contact pages and/or toll-free telephone numbers • Stakeholder surveys • Stakeholder advisory councils • Collaboration through third-parties such as participation in scientific or industry outreach programs or activities		X	X	X
2. Stakeholder engagement plans should include mechanisms for giving feedback or following up on input after engagement. **Guidance:** ▪ A summary of stakeholder engagement and resulting actions should be posted on the organization's website or otherwise made publicly available.		X	X	X
3. Make publicly available a summary of the feedback and actions being taken, if any, as a result of stakeholder engagement. A public summary of stakeholder feedback must respect a stakeholder's desire for their feedback or identity to remain confidential. **Guidance:** ▪ Post of summary of input received and resulting actions on the organization's website. ▪ If feasible, distribute a summary of input received and resulting action to be taken to stakeholder participants.		X	X	X

B. Stakeholder Engagement Commitments *(cont.)*

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
4. Provide opportunities for both collaborative stakeholder engagement as well as engagement with individual organizations. **Guidance:** ▪ Collaborative engagement may include participation in trade, professional or consumer meetings, workshops, conferences or other opportunities for engagement ▪ Individual organization engagement includes an opportunity for feedback and engagement on products, applications or programs specific to a company or organization		X	X	X
5. Provide mechanism and process for questions or concerns. **Guidance:** ▪ May include a website, mailing address, email or toll-free number mechanisms for reporting.			X	X
6. Solicit post-market introduction input from stakeholders on impacts/benefits of gene-edited products and make publicly available a summary of the feedback and actions being taken, if any, as a result. A public summary of stakeholder feedback must respect a stakeholder's desire for their feedback or identity to remain confidential. **Guidance:** ▪ At minimum, solicit and review input for two years after a new product introduction.				X

C. Safety and Quality Commitments

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
1. Create a culture of safety so that everyone, at all levels of the organization, understands the critical importance of safety and quality. **Guidance:** ▪ Examples of verifiable evidence may include: establishing safety training courses and documenting completion by employees, developing Standard Operating Procedures specific to the development of gene-edited products, and/or engaging a third-party safety consultant or regulatory agency.	X	X	X	X
2. Compliance with the federal, state and local animal welfare laws as well as adoption of best practice guidelines to ensure appropriate health and well-being of animals involved directly in research (e.g. for feeding or nutritional studies) and as potential end-products. **Guidance:** ▪ Best practice guidelines include but are not limited to "The Guide for the Care and Use of Agricultural Animals in Research and Teaching" (FASS – Federation of Animal Science Societies) and "Guide for the Care and Use of Laboratory Animals" (National Research Council).	X	X	X	X
3. Processes or products derived from gene editing should meet or exceed local, state and national laws and standards for environmental protection. **Guidance:** ▪ Compliance with applicable local, state and federal environmental regulations, such as U.S. Environmental Protection Agency		X	X	X
4. Processes or products derived from gene editing should meet or exceed local, state and national laws and standards for food safety. **Guidance:** ▪ Compliance with applicable local, state and federal food safety regulations, such as U.S. Food and Drug Administration and U.S. Department of Agriculture		X	X	X

C. Safety and Quality Commitments *(cont.)*

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
5. Products are deemed fit for purpose through performance evaluation and testing. **Guidance:** ▪ "Fit for purpose" includes standard evaluations such as: • Geographic and production system adaptation • Performance characteristics, relative to existing commercial hybrids/varieties/breeds/strains • Processing characteristics appropriate for that crop or species, such as milling for wheat, sugar yield for sugar beets, oil quality for canola and sunflower or storage characteristics for fruits and vegetables • End-user characteristics (as appropriate for that crop or species), such as protein content for soybeans, bread-making characteristics for wheat, cooking quality for rice, flavor characteristics for fruits, and compositional characteristics of meat and milk ▪ Other helpful guidelines and best practices may be found in the ASTA Guide to Seed Quality Management		X	X	X
6. Ensure human health and safety of those engaged in gene-editing processes through conformance with standard laboratory practices as defined by the research organization and appropriate oversight agencies. **Guidance:** ▪ May include institutional or local safety policies. ▪ Includes compliance with applicable regulatory requirements such as Occupational Safety and Health Administration guidelines.	X	X		
7. Effectively implement biosafety protocols for laboratory, contained facility and field research involving experimental gene-edited organism to minimize the potential for inadvertent release of the organisms from containment. **Guidance:** ▪ Organizations should have a commitment to adopt best practices tailored to organism and application, recognizing those practices may change as technology evolves. ▪ Research organizations should have an institutional biosafety lead whose responsibilities need not be restricted to gene editing research. For academic institutions this may be an Institutional Biosafety Committee. Other organizations should have an individual, team or functional area that provides biosafety oversight of gene editing research. *(Cont.)*	X	X	X	X

C. Safety and Quality Commitments *(cont.)*

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
▪ Best practices include protocols for general biosafety; laboratory, greenhouse or facility access; recordkeeping; control of undesired species; decontamination and inactivation of research materials; and avoiding unintended transmission or releases. ▪ A useful reference is the "NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules" for suggested protocols at Biosafety Level 1. Specifically, Appendix G of the NIH Guidelines covers physical containment for standard laboratory experiments; Appendix L lists physical and biological containment conditions and practices suitable for greenhouse experiments with plants; and Appendix M specifies containment and confinement practices for research involving whole animals and experiments involving gene-edited microorganisms tested on whole animals. ▪ Another useful reference is the ASTA Guide to Seed Quality Management Practices Module 2: Breeding or evaluation in greenhouse or other contained facility and Module 3: Working in seed laboratories or storage facilities. The modules provide guidance for identifying product integrity and control concerns; determining control points to manage plausible safety concerns, if any; establishing preventative measures, monitoring procedures, corrective measures and verification procedures; and establishing record keeping and documentation procedures. ▪ A Practical Guide to Containment - Plant Biosafety in Research Greenhouses is a reference on appropriate biosafety and containment guidelines for research conducted in greenhouses. ▪ For plant field trials, best practices include protocols in the ASTA Guide to Seed Quality Management, specifically Module 4: Breeding in the field, for identifying product integrity and control concerns; determining control points to manage plausible safety concerns, if any; establishing preventative measures, monitoring procedures, corrective measures and verification procedures; and establishing record keeping and documentation procedures. ▪ For animal field trials, see FDA Draft Guidance #187 for Industry "Regulation of Intentionally Altered Genomic DNA in Animals" which covers shipments in interstate commerce of new animal drugs for tests in vitro and in laboratory research animals and for clinical investigation in animals. In general, the Investigational New Animal Drug regulations specify labeling and record-keeping requirements, animal disposition, and conditions under which food from animals used for clinical investigations can be introduced into the food supply.	X	X		

C. Safety and Quality Commitments *(cont.)*

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
8. While the likelihood of off-target changes to the DNA is low, protocols used for gene editing should be developed to limit the potential for off-target edits. **Guidance:** ▪ As gene editing technology evolves, so does the ability to further limit off-target edits. Those involved in gene editing should stay current with the latest research applicable to their specific gene editing technology to limit off-target edits.	X	X		
9. Implement appropriate processes to characterize the intended edit(s) and remove undesirable phenotypes from the gene-edited plant, animal or microbe or other organism. **Guidance**: ▪ Practices to implement include: Confirm the intended edit was made. • Use current bioinformatic tools to predict potential off-target edits. • Characterize potential off-target edits with likely phenotypic consequences based on best available information. Commercially desirable or neutral phenotypic traits can be preserved, others will be discarded or eliminated. • Confirm that the gene editing reagents were removed.		X		
10. If required, products are tested, labeled, and commercialized in accordance with existing regulatory requirements.			X	X

D. Trade and Market Considerations

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
1. Prior to commercialization, conduct a market and trade assessment appropriate to the gene-edited product that anticipates and considers the potential domestic and international impacts on relevant stakeholders up and down the value chain. **Guidance**: ▪ Best practices include identifying key production countries and potential import markets, prior to the commercialization of any new gene-edited product. As part of the market and trade assessment, consult at an early stage with the value chain for the specific crop, species, microorganism or product. ▪ Useful references include: • BIO Product Launch Stewardship Policy and Annexes • CropLife International Product Launch Stewardship • Trade and export associations can provide information and resources to assist in conducting the market and trade assessment, in particular for potential import market requirements.		X		
2. Develop and implement management plans that enable the flow of goods and support issues identified in the market and trade assessment. Follow best practices to restrict inadvertent or accidental presence of gene-edited products in the agricultural supply chain. **Guidance:** ▪ Useful references include: • BIO Product Launch Stewardship Policy and Annexes • CropLife International Product Launch Stewardship • ASTA Guide to Seed Quality Management • ASTA Guide to the Evaluation of Gene-edited Plants, or the equivalent, relevant industry reference		X	X	

D. Trade and Market Considerations *(cont.)*

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
3. Undertake early and regular consultations with relevant stakeholders while conducting the trade and market assessment and while developing and implementing the management plan. **Guidance:** ▪ Relevant stakeholders should include representatives across the value chain. For example, foodservice and retail organizations, industry associations and trade and export groups. ▪ The nature of information-sharing and communication may be different depending on crop, animal or microorganism/ product-type and commercial reach of the company, supply chain, markets and potential end-users. ▪ Useful references include: • BIO Product Launch Stewardship Policy and Annexes • ASTA Best Practices: Seed Industry Information-Sharing for Products of Gene Editing		X	X	
4. Manage product introductions so they allow for the choice of different forms of agriculture that support coexistence. Coexistence is the practice of managing different quality characteristics in a way that enables different value chains to operate and restrict accidental or inadvertent comingling and thereby possibly compromising economic value. **Guidance**: ▪ Useful references include: • BIO Product Launch Stewardship Policy and Annexes		X	X	
5. Meet applicable regulatory requirements in key countries with functioning regulatory systems identified in the trade and market assessment prior to commercialization of a new gene-edited product in the United States. **Guidance:** ▪ Useful references include: • CropLife International Product Launch Stewardship		X	X	

E. Social Considerations

Framework participants commit to:

Res = Commercial research | Dev = Commercial development stage
Sale = Commercial sale stage | Life = Product lifecycle stage

Commitments	Res	Dev	Sale	Life
1. Consider relevant potential social considerations of using gene editing by completing the Social Considerations questionnaire at an organization level. **Guidance:** ▪ Optional: an organization may complete the questionnaire for an individual application or product being developed with gene editing and voluntarily disclose their deliberations for that specific product or application. This is recommended for any new trait or application which may raise concerns among stakeholders due to its unique nature or potential impacts, positive or negative. This is an opportunity to communicate unique benefits as well as address potential concerns.	X	X	X	X
2. Verification confirms questionnaire was completed.	X	X	X	X

F. Continuous Improvement Commitments

Framework participants commit to:

Commitments	Res	Dev	Sale	Life
Framework Performance 1. Provide input and feedback on the framework, suggesting revisions as needed over time to maintain relevance with evolving technologies, best practices and stakeholder expectations. **Guidance:** ▪ Feedback on the framework should be provided to the Framework Oversight Committee to be considered and incorporated as appropriate as determined by the framework oversight body and leadership.	X	X	X	X

G. Verification Commitments

Framework participants commit to:

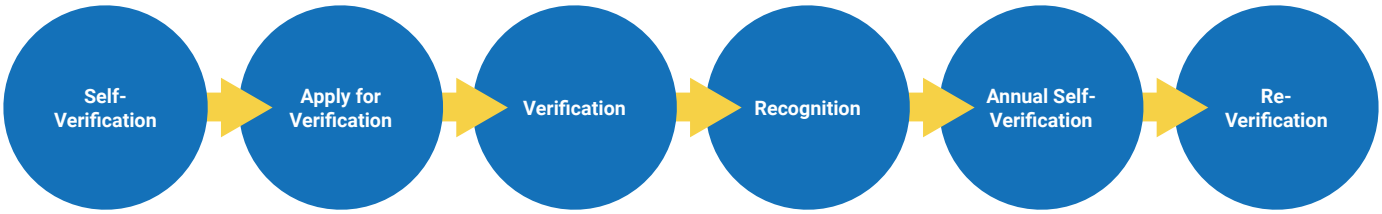
Commitments	Res	Dev	Sale	Life
1. Conduct self-assessment of conformance with Principles and Commitments, and submit assessment on an annual basis. **Guidance:** ▪ Guidance and a Self-Verification tool will be provided.	X	X	X	X
2. Submit organization's processes to comply with the framework for review by a Verifying Body. **Guidance:** ▪ See Verification Process for specifics.	X	X	X	X

THE VERIFICATION PROCESS

Organizations wishing to be recognized for conformance to the Responsible Use Framework must apply to join the Coalition as a Framework Participant. Any corporation, business or academic or governmental organization that utilizes gene editing and/or its outputs in the commercial research, development or manufacture of food and agricultural products is qualified to apply. On the Membership Form, the applicant must identify the types of activities it undertakes that will be subject to the Responsible Use Framework, i.e. its "verifiable operations".

Organizations may apply for verification for any of four development stages, requesting review of processes in place to put the principles and commitments of Responsible Use of Gene Editing into practice. Verification will be at an organization - not trait or product – level, unless otherwise requested. Organizations may elect to have a trait or product verified at additional cost. Each stage is defined in the Definitions.

High Level Verification Process Flow



System Level Verification

Verifications are performed at the Systems or Organizational level. The verifier is expected to verify and document, by examination of objective evidence, if the organization has established and implemented appropriate processes consistent with the principles and commitments outlined in the Framework for Responsible Use of Gene Editing.

Organizations will apply to the Framework Oversight Committee to request review and recognition of their conformance with the Responsible Use Framework. Once an application has been submitted, the Verifying Body shall facilitate review of the application, and if complete, facilitate completion of the verification process within six months.

The participant application will include general organization information, the primary verification contact, suggested timing for verification to be complete, and the development stages engaged in by the organization. The application includes a section for the Framework Oversight Committee to approve the application when complete. At that stage, the organization can move to the next phase of the verification process.

A key resource includes a basic training document "A Guide to Achieving Verification." It is critical that both the verifier and the organization being verified are clear on process and scope to avoid miscommunication and inefficient use of time, from either party, during verification.

Verification Phases

The verification process will include a **preparation phase**, an **opening meeting**, a **collection and sampling phase**, and a closing meeting.

The **preparation phase** is the initial contact between the verifier and the organization and gives them the opportunity to open communication channels, discuss the scope of the verification, confirm timing, who from the organization may be expected to participate, and share appropriate documents and records. From this meeting the verifier will prepare a Verification Plan which outlines the verification objectives, the verification criteria and any reference documents (framework, checklists, etc.), scope, time and length of verification, and confidentiality arrangements.

The actual verification will include the **opening meeting** to confirm what is outlined in the Verification Plan, explain the process for conducting the verification, confirm communication channels, and provide the verifier and the organization an opportunity to ask any questions.

The **collection and sampling phase** is when information relevant to the objectives, scope and criteria of the verification will be collected by appropriate sampling and then verified. Only information that is verifiable may be used as evidence. Records, procedures and processes that are used to document, establish and/or verify systems or processes relevant to the subject of the verification will be sampled. Evidence should be evaluated to determine whether the principles and commitments outlined in the framework are being met or are in place. Determinations and their supporting evidence should be recorded and then reviewed with the organization to obtain acknowledgement that the evidence is accurate and that the determinations are understood. Every effort should be made to resolve any differences of opinions concerning the evidence and/or determinations, and unresolved points should be recorded.

The **closing meeting** is an opportunity for the verifier to present initial findings, record and discuss any differences of opinion and try to resolve them. The organization may ask any clarifying questions or present additional objective evidence during this phase and verifier should confirm next steps and timing of a completed Verification Report.

A Verification Checklist is used to assure an efficient process. This will establish the appropriate questions for verifiers to ask that will enable them to determine whether or not an organization is meeting its framework commitments. This includes sections for the verifier to record objective evidence, make notes, and signal an initial determination.

Key resources related to this part of the process include guidance, based on the framework, which is intended to assist the organization in meeting their framework commitments. Basic guidance is included in the "Guide for Achieving Verification." Note that this guidance is not intended to be prescriptive, but rather provide more detailed explanations of the commitments and examples on how they may be met with objective evidence.

Meeting the commitments can be achieved in a variety of ways beyond those described in the guidance. This Guide ensures that the verifier and participant understand both process and expectations during verification.

There can be occurrences when the participant disagrees with a determination by a verifier. All effort should be made to resolve this difference prior to submission of the report by the verifier to the verification body. When an agreement cannot be reached, the Dispute Resolution Process will be used to resolve the issue.

Organizations must verify that they are still in conformance via a self-verification on an annual basis, and complete a full re-verification every three years, or following any change in ownership or major restructuring which could impact conformance with the framework. Re-verification will include documentation or evidence of actual implementation of the organization's processes and policies that support the principles.

Self-Verification, Re-Verification Cycle

Recognition

Once approved, applicants will receive a letter and certificate of conformance with the Framework for Responsible Use of Gene Editing and may use such designation in marketing, business correspondence or other communications. Any use of conformance claims on product packaging or labels is currently prohibited.

Successful completion of requirements will be communicated from the verification body to the Coalition. As determined by the Framework Oversight Committee the recognition of successful completion will be conferred to the participant. A recognition and use policy includes examples of appropriate and inappropriate ways in which recognition may be publicized. Any use must NOT infer a guarantee of anything related to specific products developed by the participant, including guarantees related to safety of the product, efficacy of the product, impact on trade, or compliance with applicable regulations.

SOCIAL CONSIDERATIONS QUESTIONNAIRE

Using the questionnaire

In this section you will find questions designed to help you consider potential social considerations related to the use of gene editing. Carefully considering the questions and exploring different perspectives assures a broader view of the technology and its potential implications, both perceived and actual. This process will help organizations better engage in dialogue about the technology and consider stakeholder perspectives when making decisions. The process may also help communicate more clearly about the decision to use the technology. The social considerations questionnaire is an opportunity to communicate social benefits (positive impact on natural resources, enhanced animal well-being, etc.) as well as address potential concerns (limited access to benefits, negative impact on bio-diversity, etc.).

Consideration of these topics is likely already occurring as part of strategic planning, product development, corporate or social responsibility or other functions, and as part of stakeholder engagement activities. This section of the framework provides the opportunity to acknowledge that these discussions are happening internally and/or with external stakeholders, within your organization and/or through an industry association. All activities which contribute to understanding stakeholder perspectives may be included here.

The depth and scope of social considerations will vary by organization depending on the anticipated use and applications of gene editing and may change over time. Social consideration conversations are an opportunity to communicate unique benefits as well as address potential concerns, especially when considering novel or unique applications.

Responses on the Social Considerations Questionnaire are intended to be at the organizational, not the application, level. You may elect to provide application-specific information if you choose, but it is not required. The responses should be consistent with how the organization analyzes impacts of their product portfolio – if your organization only assesses impacts at the organization level, then complete the questionnaire at that level. If it is done for a particular product (e.g. gene-edited wheat), or for a unique or novel application, then you may include responses at that level.

We suggest you consider each question and the prompts supplied from the perspective of different stakeholders. The questions and prompts in the questionnaire and guidance document are not intended to be an exhaustive list of all potential topics. Please consider topics specific to your organization that may not be captured in the examples. You may opt to gather input directly from stakeholders to help you prepare to complete the questionnaire. When completing the questionnaire, consider a broad a range of perspectives, taking into account different experience and understanding, levels of awareness of gene editing and value systems.

For each question, take time to consider the different opportunities and potential topics that stakeholders may raise. Is this an opportunity to highlight benefits that may not have been considered before, or address areas of concern? Remember, there are no right or wrong answers, and there will never be consensus. The goal is to demonstrate you are engaging stakeholders in discussion about social considerations of gene editing.

SOCIAL CONSIDERATIONS QUESTIONNAIRE

Please use this template to complete the Social Considerations Questionnaire.

1. Use the Explanation of Factors and Potential Questions to Consider columns to stimulate discussion and/or stakeholder engagement, and as a guide to the type of information to address in the summary column.
2. To assist in the Social Considerations, several potential topics for each factor are provided below. These are examples designed to demonstrate the range of topics or questions that may be considered. Your responses will vary depending on your organization's anticipated use and applications of gene editing. Not all factors or topics will be relevant to your organization. Your responses should be at the organizational, not the application, level. You may elect to provide application specific information if you choose, but it is not required.
3. Summarize the outcomes of your considerations and/or stakeholder engagement in the far right column. This is intended to be a high level summary; supplemental documents or resources may be referenced or included as attachments at your discretion.

FACTOR	EXPLANATION OF FACTORS	POTENTIAL QUESTIONS TO CONSIDER	SUMMARIZE THE OUTCOMES OF YOUR CONSIDERATIONS AND/OR STAKEHOLDER ENGAGEMENT
Purpose of utilizing the technology (Social responsibility)	What's the purpose of using gene editing? What is the benefit of using gene editing vs. other breeding methods or other approaches?	• What is the organization's mission and how does gene editing support that mission? • How does gene editing fit into the organization's business objectives and values? • Why was gene editing selected as the breeding method? Why is gene editing being used instead of conventional methods? What is the benefit of using gene editing? Could this be accomplished with conventional methods? • Who benefits from the use of the technology – farmers, food manufacturers, consumers? • Have you considered the socio-economic costs associated with gene editing versus other methods? • How will your company address social considerations?	

FACTOR	EXPLANATION OF FACTORS	POTENTIAL QUESTIONS TO CONSIDER	SUMMARIZE THE OUTCOMES OF YOUR CONSIDERATIONS AND/OR STAKEHOLDER ENGAGEMENT
Potential impacts, positive or negative, of the various applications of gene editing and gene-edited products developed by your organization for **environmental sustainability** (incl. natural resources)	Describe the potential consequences that you have considered (positive, negative or neutral) of gene editing, or gene-edited products developed by your company or organization, on agricultural resources, ecosystem functions and biodiversity. Are the broad consequences likely to be different from other options available to address the same challenge?	• What are the impacts to biodiversity in target species and other species dependent upon the target (ex: pests), if any? • What are the environmental impacts, positive or negative, on other inputs in the system? Will it result in a shift of resource use or need for land, water and inputs? • How long are the sustainability gains likely to last? What systems would need to be implemented to make the sustainability gains last longer?	
Potential impacts, positive or negative, of the various applications of gene editing and gene-edited products developed by your organization for **economic sustainability** (incl. economic resources)	Describe the potential consequences that you have considered (positive, negative or neutral) of gene editing, or gene-edited products developed by your organization, on rural and food production economies. Are the consequences likely to be different from other options available to address the same challenge? How would users or others access the technology? Have you considered the impact on the downstream supply chain and consumer choice?	• Are economic resources used in the value chain affected positively or negatively by the use of gene editing? • Does use of the technology increase or decrease reliance on a specific resource? • Does it maximize the value of inputs? • Does the use of gene editing or gene-edited products impact efficient use of resources, and if so in what way? • Will downstream producers and supply chains need to adjust to accommodate the use of the technology and could there be costs associated with that? • Will the use of the technology impact conventional products and their marketing? How might this impact choice for farmers or consumers?	

Factor	Considerations	Relevant Yes/No	Explanation/Support
Potential impacts, positive or negative, of the various applications of gene editing and gene-edited products developed by your organization for **food production systems**	Describe the potential consequences that you have considered (positive, negative or neutral) of gene editing, or gene-edited products developed by your organization, on ag/ food production practices and economics. Are the consequences likely to be different from other options available to address the same challenge?	• How does using the technology enhance the productivity and well-being of the food value chain? • What processes are in place, if needed, to monitor and act on potential impacts? • What special stewardship or IP may be needed to avoid impacts on trade or food production systems? • How might different consumers react to the products produced by your company and what information might be relevant to those questions?	
Potential impacts, positive or negative, of the various applications of gene editing and gene-edited products developed by your organization for **food animal welfare**	Describe the potential consequences that you have considered (positive, negative or neutral) of gene editing, or gene-edited products developed by your organization, on the welfare of gene-edited animals or on food animals that consume them. Are the consequences likely to be different from other options available to address the same challenge?	• Does using the technology impact the welfare of food animals? • What processes are in place to monitor and act on potential impacts, if needed? How are they being managed? • Does the use of the technology change the need for or type of inputs for animal production? • Have you considered how the use of gene editing interacts with other strategies to improve animal welfare?	

LEGAL DISCLAIMER

The Framework for Responsible Use of Gene Editing in Agriculture is a tool to assist program participants in building trust in gene editing with stakeholders. The Framework is designed to be flexible and its application will differ according to the size, nature and complexity of the organization and products involved.

This Framework is not, and should not be used as, a substitute for (1) a user's own individual understanding of its legal requirements, (2) consultation by a user with its legal counsel and other advisors, or (3) direct contact with appropriate regulatory agencies.

The Framework Guide does not define or create legal rights or obligations, and the Center for Food Integrity (CFI), author of and administrator of the Framework, specifically disclaims any such rights or obligations. CFI does not make any warranties or representations, either express or implied, with respect to the accuracy or completeness of the information contained in this document, or the sufficiency of the general procedures and processes contained herein to eliminate risk inherent in the referenced operations or processes; nor do they assume any liability of any kind whatsoever resulting from the use of or reliance upon any information, procedures, conclusions, or opinions contained in this document. CFI assumes no responsibility to update this Framework.

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