GES CENTER

NC STATE UNIVERSITY

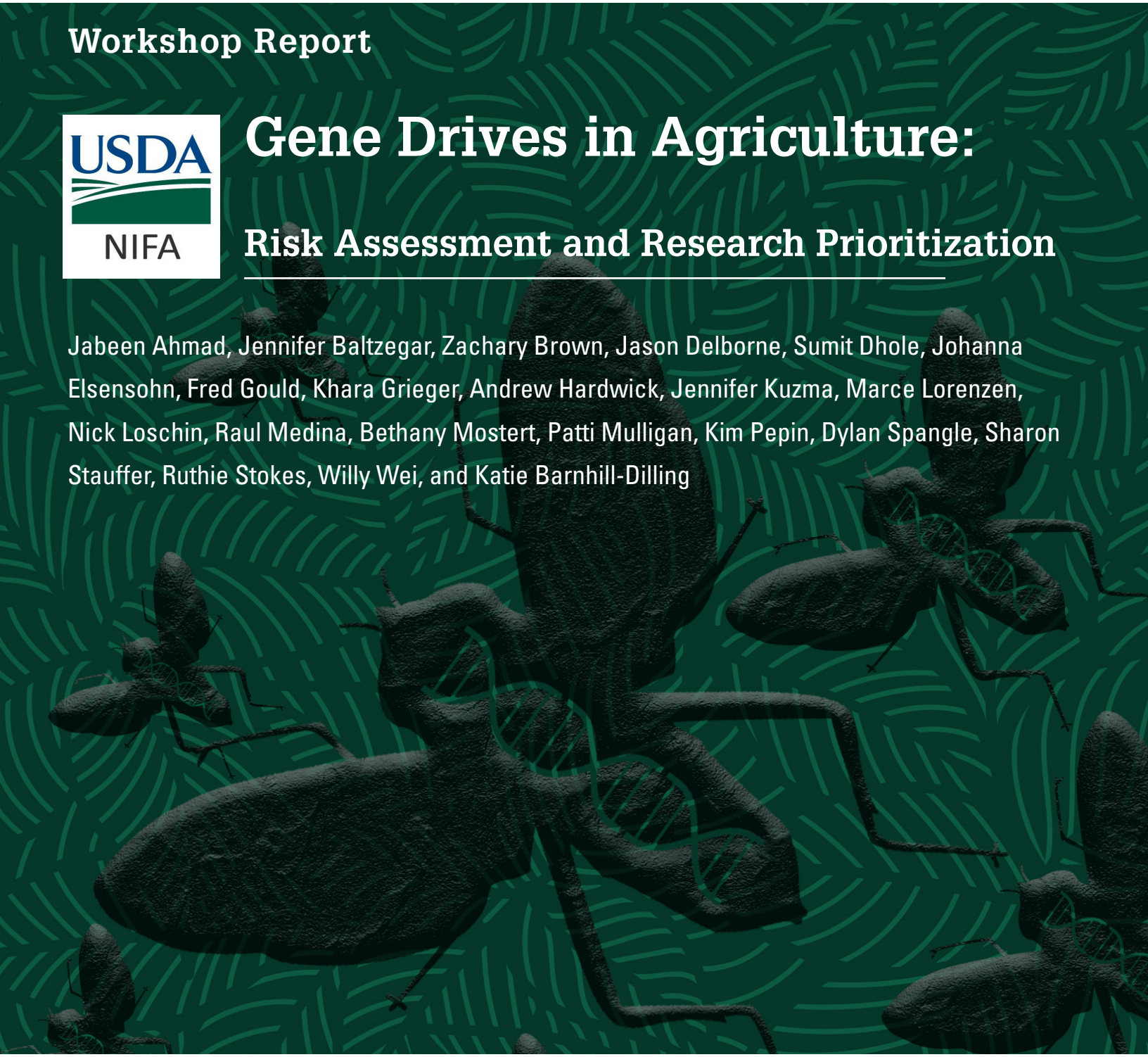
Workshop Report

USDA NIFA

Gene Drives in Agriculture:

Risk Assessment and Research Prioritization

Jabeen Ahmad, Jennifer Baltzegar, Zachary Brown, Jason Delborne, Sumit Dhole, Johanna Elsensohn, Fred Gould, Khara Grieger, Andrew Hardwick, Jennifer Kuzma, Marce Lorenzen, Nick Loschin, Raul Medina, Bethany Mostert, Patti Mulligan, Kim Pepin, Dylan Spangle, Sharon Stauffer, Ruthie Stokes, Willy Wei, and Katie Barnhill-Dilling



Genetic Engineering and Society Center, NC State University

Integrating scientific knowledge and diverse public values in shaping the futures of biotechnology

Online at: go.ncsu.edu/ges-gene-drive-workshop-white-paper

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Gene Drives in Agriculture

Workshop on Risk Assessment and Research Prioritization

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Executive Summary

The Genetic Engineering and Society (GES) Center at North Carolina State University (NC State) hosted an online workshop entitled "Gene Drives in Agriculture: Workshop on Risk Assessment and Research Prioritization" on June 2, 3, and 17, 2022. The workshop was funded by the USDA-NIFA Biotechnology Risk Assessment Grant program (grant number 2020-33522-32269; PI = Barnhill-Dilling), with additional support from and partnership with the NC State Center for Excellence in Regulatory Science for Agriculture (CERSA). The workshop included an interdisciplinary lineup of speakers brought together in an effort to review and develop risk assessment methodology associated with gene drives for agriculture pest control. This report was generated to inform and summarize foreseen risks associated with gene drive technology for agriculture pest control to identify data needs for gene drive technology.

The workshop featured panelist experts in multiple disciplines specializing in gene drives, risk assessment, policy, and agricultural pests. By use of presentations and breakout sessions, many ideas were presented regarding the risk assessment and risk governance of gene drives in agriculture. This workshop report does not represent the opinion of all the participants in the workshop but serves as a bridge to cover multiple perspectives from interdisciplinary efforts. This report is structured as:

1. An overview of the workshop
2. Background on gene drive and potential applications
3. *Drosophila suzukii* case study
4. Risk assessment for gene drive
5. Regulatory framework for biotechnology and gene drive in the U.S.
6. Potential risks (as identified by workshop participants)
7. Data needs (as identified by workshop participants)

1.0 Workshop Purpose

On June 2, 3, and 17, 2022, the Genetic Engineering and Society (GES) Center at North Carolina State University in Raleigh, North Carolina, in partnership with the Center of Excellence in Regulatory Science for Agriculture hosted the "Gene Drives in Agriculture: Risk Assessment and Research Prioritization" online workshop. The workshop was conducted in association with a USDA/NIFA-funded grant in the Biotechnology Risk Assessment Grant program, entitled "Informing a Risk Assessment Research Strategy for Gene Drive Agricultural Applications through Interdisciplinary Dialogue and Exchange" (grant number 2020-33522-32269; PI=Barnhill-Dilling). The workshop brought together a diverse group of experts from academia and government agencies to explore **risk assessment** and data needs for the development of **gene drive** technology for agricultural pest management.

In 2015, the GES Center hosted an international workshop that identified research and governance needs for gene drives which was funded by the NSF; and from it produced a journal volume, including several papers on agricultural gene drives (Delborne et al., 2018). However, the focus of this previous workshop was not specifically on risk assessment, and gene drive technology has advanced considerably since. In addition, a 2016 National Academies of Science, Engineering and Medicine (NASEM) report called "*Gene Drives on the Horizon*" recommended continued research on the potential benefits and risks of developing gene drive technology for **agricultural pests**. Therefore, this workshop focused on identifying research needs related to risk assessment of gene drive technologies, drawing from a range of perspectives and disciplines. Information collected and synthesized from the workshop is presented in this report with the goal of informing risk assessment research priorities and data needs regarding gene drive technology in agricultural pest management.

1.1 Background

Technological advancements involving gene drive applications in agriculture are proceeding rapidly. Potential and in-progress gene drive systems include *Drosophila suzukii* and *Diaphorina citri*, which feed on soft-skinned and citrus fruits, respectively. Despite developments in gene drive technology, there are gaps in governance systems and challenges to acquiring underlying data for risk assessments. Furthermore, there are few risk assessments with studies on public perceptions and acceptance. Heeding these past lessons learned from agricultural biotechnology and enhancing risk assessments through informed interdisciplinary engagement are important considerations. Interdisciplinary exchanges may also help ensure that responsible research and innovation is realized in the case of gene drive applications in agriculture. In essence, diverse and multi-stakeholder conversations should be conducted alongside research endeavors aimed to conduct risk assessments for gene drives. This workshop aims to inform risk assessment research strategies for gene drive agricultural applications through interdisciplinary dialogue and exchange with diverse experts.

While research funding is undoubtedly important to address environmental health and safety risks, it is also critical to establish a coordinated research strategy to acquire appropriate data in which to make informed governance decisions. Previous work has examined what a research agenda for the ecological implications of synthetic biology should entail, including the recent NASEM "*Gene Drives on the Horizon*" report. While many have called for interdisciplinary engagement to inform risk assessments, there has been limited study on what an interdisciplinary risk research agenda should entail, specifically for gene drive use in agriculture.

Moreover, we are aware of only one study which has examined public perceptions and/or acceptance of utilizing gene drives for agricultural purposes (Jones et al., 2019). While the study suggests that the majority of the U.S. public would support the limited use of some agricultural gene drives (e.g., that target non-native species damaging crops with failing and costly conventional control options), the study also suggests that gene drives that spread freely have considerably less support. Jones (2019) also examined what respondents believe to be the "most and least important uncertainties to resolve before deciding whether gene drive insects should be used to control pest damage to crops" with human health effects and environmental consequences of pest removal ranking the highest. Following best practices for biotechnology, oversight, public perceptions, and support of gene drive applications in agriculture will need to be considered and factored into risk-based decision-making.

1.2 Workshop Objectives

1. Have interdisciplinary dialogue and exchange on key risk assessment research needs for gene drive technologies for agricultural pest management;

2. Elicit a range of stakeholder perspectives regarding gene drive risk assessment and summarize research needs related to gene drives for use in agriculture; and
3. Identify research and data needs on gene drive technologies for agricultural pest management and categorize needs as short-, medium- or long-term research priorities.

1.3 Workshop Design

The workshop was designed to foster a conversation and dialogue between diverse stakeholders in order to identify risk assessment and associated data needs related to gene drives in agricultural pest management. Workshop participants came from academia, government, industry, and nonprofits, representing diverse areas of expertise as described in Figure 1. The first day of the workshop consisted of presentations introducing gene drive technologies, agricultural pests, and the use of gene drives for agricultural pest management. The second day consisted of focus group discussions on identifying risk assessment and data needs and ranking priority needs based on the short, medium, and long term. Finally, the third day of the workshop consisted of reviewing outputs from the first two days and gathering additional insights and feedback from workshop participants on risk assessment needs. This report was then drafted after the second day and discussed during the third day of the workshop. A detailed agenda of the workshop can be found in Section 1.4. All participants and speakers were invited to review and add content to the report.

Figure 1 Expertise of workshop participants.

1.4 Workshop Agenda

Day 1: June 2, 2022, 12-4pm ET		
12:00-12:15pm	Introduction & Overview of the Workshop	Katie Barnhill-Dilling, NCSU
12:15-12:45	Overview of Gene Drives in Agriculture	Fred Gould, NCSU
12:45-2:00	Risk Assessment Panel	John Mumford, ICL
		Kim Pepin, USDA
		Lisa Knolhoff, USDA
	Facilitated Discussion with Panelists	
2:00-2:15	Break	
2:25-2:45	Diamondback Moth Case Study	Tony Shelton, Cornell Univ.
2:45-3:15	Drosophila suzukii Case Study	Johanna Elsenson, USDA
3:15-4:00	Facilitated Discussion about Cases and Next steps	

Day 2: June 3, 2022, 12-3pm ET		
12-12:30	Overview of Day 1 and Introduce Goals	Katie Barnhill-Dilling, NCSU
12:30-1:15	Breakout Sessions Identify key data requirements to complete a risk assessment for gene drive uses relevant for U.S. agricultural systems Categorize identified data requirements according to near- (within 5 years), medium- (5-15 years), and long-term (>15 years).	
1:15-2:45	Plenary Sessions Breakout session results Round robin: priority data needs	
2:45-3:00	Next Steps and Writing Process	

Day 3: June 17, 2022, 12-2:45pm ET		
12:00-12:15pm	Overview of Day 3 and Summary of Workshop Report Draft	Katie Barnhill-Dilling, NCSU
12:15-12:30	Background to the Issue	Jabeen Ahmad, NCSU
12:30-12:35	Question & Answer for Section 1	
12:35-12:40	Regulatory Context	Andrew Hardwick, NCSU
12:40-12:45	Question & Answer for Section 2	
12:45-1:00	Identified Risks	Bethany Mostert, NCSU
1:00-1:15	Breakout Room Discussion on Section 3	
1:15-1:30	Question & Answer for Section 3	Bethany Mostert, NCSU
1:30-1:50	Section 4, Data Needs	Dylan Spangle, NCSU

1:50-2:10	Breakout Room Discussion on Section 4	
2:10-2:25	Question & Answer for Section 4	Dylan Spangle, NCSU
2:25-2:35	Preliminary Conclusions	Ruthie Stokes, NCSU
2:35-2:45	Summary and Next Steps	Katie Barnhill-Dilling, NCSU

2.0 Background on Gene Drives

2.1 What Is a Gene Drive?

Genes that have super-Mendelian inheritance are said to have "drive" or to be "selfish." These types of genes are able to increase in frequency and spread through populations by employing genetic mechanisms that are capable of circumventing Mendel's laws of inheritance. (Burt 2003, Esvelt 2014). Gene drives may be co-opted to introduce desired traits into a population, but they may also be used to spread traits with negative fitness costs. While there are different methods to create gene drives, most are now based on **CRISPR/Cas9** technology (Esvelt 2014).

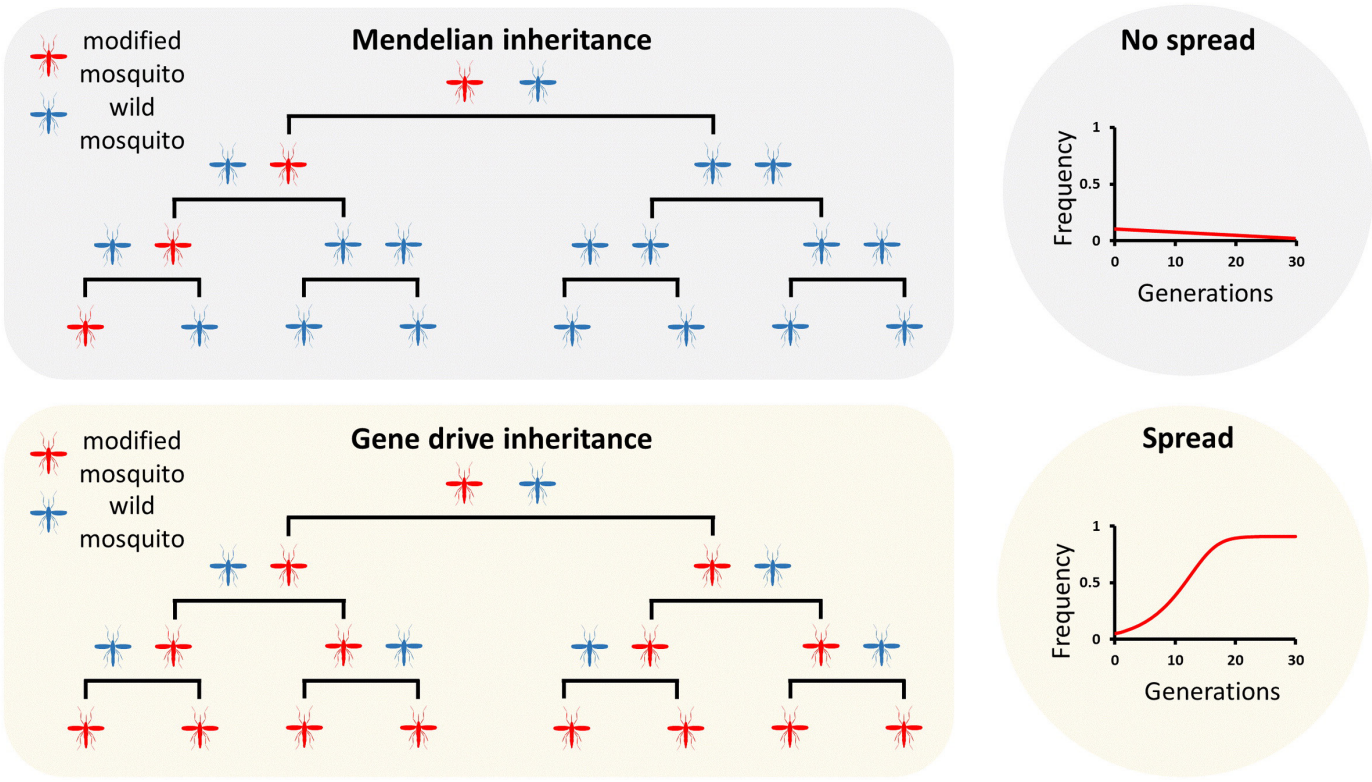

Figure 2 Mendelian inheritance vs. gene drive inheritance (Hammond & Galizi 2017)

2.2 Gene Drive Types and Uses

Gene drives can be categorized as either unrestricted or restricted. **Unrestricted gene drives** continue to spread once they are introduced and do not have a mechanism by which they can be limited. **Restricted gene drives** are limited in scope temporally, spatially or by both. These drives

may spread in a specific area and stay there (**spatial restriction**) or disappear after a period of time (**temporal restriction**). The type of gene drive is an important consideration because they present different risks and require different data needs and prioritization. Whether unrestricted or restricted, gene drives can be designed in different ways taking advantage of different genetic components. The table below provides select examples of gene drives.

Gene Drive	Description	Type	Use
Homing-based	Insertion of a gene drive nuclease with its own recognition site that cleaves DNA and then makes copies of chromosomes with the gene drive	Unrestricted	Target essential genes, drive a cargo, population suppression, population replacement
Sex distorter or Y-drive	Insertion of gene drive to change balance between sexes	Unrestricted	Population suppression by changing balance of sexes
Split	Like homing-based but components of gene drive are split between chromosomes where one spreads through drive but other through Mendelian inheritance	Restricted	Limited target populations controlled in short periods, spatially limited or threshold dependent
Maternal Effect Dominant Embryonic Arrest (MEDEA)	Gene drive involves a toxin expressed from a maternal promoter and zygotic antidote	Case dependent	Population replacement

Table 1 Selected examples of gene drives

The global gene drive proposed in Esvelt (2014) could spread through an entire species and result in permanent changes. We frequently only want to affect a pest species in a certain geographical or temporal range and avoid creating changes in the natural range. Therefore, much recent theoretical work has been devoted to designing gene drive mechanisms that may be spatially or temporally limited. (e.g., Nobel 2019, Dhole 2019, Oberhofer 2019, Champer 2020) These designs may be more acceptable as they either will not be able to spread to populations where changes are not wanted or will be lost from the population after a certain amount of time.

The two primary strategies for pest control remain: (1) **population suppression** and (2) **population replacement**. Population suppression strategies aim to decrease the number of individuals in the population, similar to what Craig (1960) envisioned. Population replacement strategies aim to change the phenotype of most individuals in the population to one that is more desirable. An example of this would be spreading a disease-refractory gene through a mosquito population that would prevent mosquitoes from spreading the diseases that they vector. In an agricultural setting, population suppression may be the preferred strategy to employ for pests that feed on crops, however population replacement may be beneficial for vectors of plant pathogens, such as the corn planthopper, the vector of maize mosaic virus.

Synthetically engineered gene drives for pest control may be useful for agricultural applications, but many milestones need to be met before gene drives can be recognized as a viable solution.

Future milestones include functional cage and field tests, risk assessments in natural settings, as well as social and regulatory acceptance. Many of these points are covered below in the discussion of data needs that we identified in the workshop.

To date, gene drives have only been created and tested in the lab, and no gene drives have been released. (e.g., Gantz and Bier 2015, Hammond 2016, Hammond 2017, Kyrou 2018, Pham 2019, Hammond 2021).

3.0 Drosophila Case Study

To examine potential issues related to the development and deployment of a gene drive insect in agriculture, the workshop included an in-depth look at the case of *Drosophila suzukii*, common name spotted wing drosophila (SWD), as one target organism for gene drive research. To date, the development of a gene drive SWD has been confined to small-scale proof of concept experimental studies. The goal of using a case study was to use a theoretical yet realistic example to elucidate specific details about issues that may arise from a gene drive approach in a specific cropping system(s).

3.1 Spotted-wing drosophila and Pest Management

Spotted-wing drosophila (SWD, *Drosophila suzukii*) is an invasive insect pest of several economically important fruit crops, most notably berries. SWD is native to east Asia and was first detected on the mainland United States in 2008. It now occurs on all continents except Antarctica and Australia. SWD females lay their eggs into ripening and ripe fruit which quickly leads to fruit decay as the larvae consume the inner fruit flesh. SWD has caused significant economic loss for much of the fruit industry, from direct crop loss, increased management costs, shipment delays due to increased surveillance, and trade restrictions that exclude certain market segments. In the U.S., conventional and organic insecticides have dominated the management of this pest since its introduction. This overreliance has led to secondary pest issues and concerns for reduced insecticide effectiveness.

3.2 SWD and Gene Drives

Gene drive technology has been proposed as a tool for population reduction for SWD due to a recognized need for effective control mechanisms to mitigate this insects' impact. Additionally, adding gene drive as a tool within an **integrated pest management** (IPM) approach could help control SWD population levels beyond farm borders as the gene drive insects would expand to all area habitats suitable for SWD like wooded and disturbed landscapes. Adding GD to current area-wide pest management efforts may be effective for insect pests that have broad host ranges and high environmental tolerability, like SWD. Currently on-farm management fails when SWD populations spike in the late summer and fall. Gene drives may offer a way to help keep SWD populations low enough so growers can manage their crops with currently available tools in the IPM arsenal.

3.3 SWD, Gene Drive Systems, Risk Assessment, and Data Needs

Considerable progress has been made toward the development of a SWD gene drive insect line modified to kill females (Schetelig 2021). However, a gene drive SWD line does not exist yet, and therefore the type of drive and mechanism of action is still unknown. The risks of a gene drive modified SWD are largely theoretical, with some risks unknowable until that insect is released into an open environment. As SWD is a potential target for a gene drive approach, there are several studies that have examined what data needs a potential risk assessment may include. The economic significance of SWD has generated a research base of knowledge on the different types of impacts and

challenges growers face across the United States. As SWD is pervasive throughout areas where it is already established, SWD is a good case study to examine the importance and viability of control mechanisms to limit the spread of a GD insect and the impact from a control failure.

For purposes of the workshop, the case of SWD was used to guide discussion and to provide a concrete example for risk assessment and to identify data needs. General dimensions of risk assessment can be applied toward other agricultural pests as well.

4.0 Risk Assessment for Gene Drives

4.1 Risk Assessment and Applications

Risk assessment is a structured process to identify, evaluate, and often quantify risk using available data and information (Aven 2018). **Risk** is commonly defined as a combination of probability and severity of consequences. While different fields may define and describe risk assessment processes slightly differently, risk assessment aims to better understand and evaluate a given risk using available data and information and is typically characterized by four main stages (hazard identification, hazard characterization, exposure assessment, risk characterization) (NRC 2009). These stages aim to understand what can go wrong from a particular hazard or threat, and if it does happen, then what are the consequences from occurrence. The stages of risk assessment are informed by different laboratory and/or field-based studies related to understanding exposures to a particular hazard as well as the potential for adverse effects that result from such exposures. Results from risk assessments can also be used to more fully understand a given risk, including relationships between exposure and the development of adverse effects, and at what level or circumstance may result in a risk. The outputs of risk assessment can include both qualitative descriptors of risk (such as 'high', 'moderate', 'low', and 'negligible'), as well as quantitative or semi-quantitative estimates of risk and taking uncertainty into consideration (NRC 2009).

Risk management decisions can be informed from results of risk assessments while also factoring in a number of other parameters to support decision making. For example, results from risk assessment can also be coupled with findings from social science studies (e.g., risk perception and acceptance studies), policy-implications, and socio-economic and cultural circumstances to inform decisions and other risk management actions. Such social input may also help to inform the scope and dimensions for risk assessments, identifying areas of concern to a range of interested groups.

We also note here that while risk assessments have been a traditional approach to understand and estimate risks in a variety of fields and disciplines (e.g. chemicals management, industrial facilities, nuclear energy plants, biotechnology), some have criticized risk assessment processes as having rather narrow framings that may not account for stakeholder perceptions and values or other forms of knowledge (Kuzma et al., 2018; Meghani & Kuzma 2018; Kuzma 2021; Hartley et al., 2022). While these criticisms exist, risk assessment still remains to be a primary tool for decision-makers and those in regulatory agencies to understand and make decisions regarding various risks, including those in biotechnology.

4.2 Risk Assessment for Agricultural Gene Drive Systems

Gene drives have a wide range of potential applications in agriculture, environmental conservation, and vector control for public health. As gene drives are designed to purposely and quickly modify the genetic material of targeted organisms, risk assessments should be conducted before

moving forward with field testing and further considerations of deployment. Risk assessments can describe potential risks, help improve risk-based decisions, and should be conducted on a case-by-case basis (e.g., Redford 2019).

As described in *"Gene Drives on the Horizon,"* (NASEM 2016) the risk assessment process for gene drives involves three phases: problem formulation, analysis, and risk characterization, which includes identification of the pathways and consequences of the risks. This is an alternative description of the four stages used in the traditional risk assessment process as described by NRC (2009) and takes into consideration protection goals and related regulations. In addition, risk assessments of gene drives also need to consider three additional and distinguishing features as described in the NASEM report (2016): *"1) a gene drive is passed on from one generation to the next at a rate greater than that described by Mendelian inheritance; (2) a gene drive construct can have effects on other parts of the organism's genome beyond the target (i.e., off-target effects); and (3) gene-drive modified organisms are designed to spread, along with their effects, into the larger environment."* (NASEM, 2016) For these reasons, comprehensive risk assessments of gene drive should also reflect the ability for the gene drive organism to distribute widely (and to **non-target organisms**), persist in the environment, and have effects on a range of ecological organisms, including and non-target and **target organisms.** These and other potential risks are described in greater detail below.

Next, risk assessment of gene drives focuses on evaluating the effects of gene drive organisms. Simulations and modeling are often used to understand potential effects, although they are also limited by the fact that they may not necessarily represent the "real world" of releasing gene drive organisms in complex ecological systems, which are often characterized by numerous additional variables. While it could be useful, the use of small size trials (or laboratory or biocontainment tests) to inform large-scale release of **gene drive modified organisms** (GDMOs) is challenging as the receiving environment could be different as well as the biotic/abiotic components that the released GDMOs may interact with. Each stage may need different strategies to generate specific data requested for risk assessment.

In summary, the risk assessment frameworks for conventional genetically modified organisms could work for gene drives with additional considerations and necessary updating (EFSA GMO Panel 2020) regarding specific characteristics and novel aspects of gene drives. The choice of parameters for comparison within the risk assessment process is also challenging. Appropriate alternative approaches for the comparison could be biological control, sterile insect technique, *Wolbachia*-mediated incompatible insect technique or genetically modified counterparts without an engineered gene drive (EFSA GMO Panel 2020).

5.0 Current Regulatory Landscape in the United States: Gene Drive Systems for Agricultural Pests

The purpose of this section is to provide background information about what risks might be considered by different federal agencies for gene drive systems for agricultural pests and how risk assessments may be done. It is important to note that at the time of this writing no application of gene drives has been evaluated by any U.S. federal agency so depending on what happens between now and when gene drive pests come under regulatory review, their regulation may fall under different agencies or different kinds of risk assessment. This section uses previous regulations of biotechnology products like the Oxitec Mosquito, the genetically engineered diamondback moth, and the genetically engineered citrus tristeza virus to give some ideas of how regulation of gene drive systems for agricultural pests might go. This section provides a broad overview of where gene drive systems for agricultural pests might fall into the U.S. regulatory landscape.

5.1 The U.S Coordinated Framework for the Regulation of Biotechnology Products

The U.S. Coordinated Framework for the Regulation of Biotechnology Products was originally created in 1986 with the goal of ensuring the safety of biotechnology products for people and the environment while not impeding innovation (EPA, FDA, USDA, *About the coordinated framework*). The Environmental Protection Agency (EPA), Food and Drug Administration (FDA), and Department of Agriculture (USDA) were brought together as lead agencies to regulate new biotechnology tools. Since then, the CFRB has been refined most recently in 2017. This update provides guidance for which lead agency would be responsible for different biotechnologies and gives tools for coordinating regulation between federal agencies. Table 2 below shows the relevant triggers of gene drive systems for agricultural pests for each lead agency based off of the 2017 update and FDA's "Guidance for Industry #187: Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs." This table is a compilation of different sources and may not match the exact language used by each lead agency.

Agency	Gene Drive Systems for Agricultural Pests
EPA	Regulated by the Office of Pesticide Program if an animal is used as a pesticide. The EPA ensures safety through the regulation of any chemical pesticide residues due to gene drive systems for agricultural pests. EPA might also have some authority for gene drives under the Toxic Substances Control Act regulations for genetically engineered microbes that are not plant pests or pesticides.
FDA	Regulated by the Center of Veterinary Medicine if the gene drive systems for agricultural pests is considered an animal drug (based on policy for "Intentionally Genomic Altered" IGA animals) as defined by the FDA and is not a genetically engineered animal that is already regulated by other government agencies or entities.
USDA	Regulated by the Biotechnology Regulatory Services (BRS) of the Animal and Plant Health Inspection Service (APHIS) if gene drive systems for agricultural pests pose a plant pest risk as defined by USDA.

Table 2 Regulatory CFRB Triggers Relevant for Gene Drive Systems for Agricultural Pests

Which lead agency under the CFRB will be required to regulate gene drive systems for agricultural pests depends upon the purpose of the product, the claims made on the product, and the properties of the gene drive systems for agricultural pests, as governed by rules or policies under each lead agency. For example, Oxitec Mosquitoes were initially regulated by the FDA before being later regulated under the EPA. The FDA provided industry guidance in 2017 that the agency would only regulate "mosquito-related products that are intended to prevent, treat, mitigate or cure a disease" and that the EPA would regulate "mosquito-related products" when the product is intended to function as a pesticide (FDA 2017; see FDA 2022 website link to guidance). Other examples of the use of biotechnology to reduce organisms associated with a plant pest risk like the genetically engineered diamondback moth or the genetically engineered citrus tristeza virus have been regulated by USDA under the Plant Protection Act as they are plant pests (APHIS, 2017, 2020). What these examples show is that which agency gene drive systems for agricultural pests might be regulated will depend upon the gene drive systems for agricultural pests' properties, the claims the developers make on the product (e.g., mosquito as pest control versus disease control), and the purpose of the product.

Each federal agency considers different risks depending on the laws that the agency uses to regulate biotechnology. For example, under the FDA New Animal Drug regulations, the agency typically

looks at safety to the animal (from the drug) and efficacy of the drug (in the case of IGAs the "drug" is the DNA introduced). Concerns have been raised as to whether this regulatory pathway for gene drives would cover the ecological risks pertinent to the environmental release of gene drives (Meghani & Kuzma 2018; Kuzma 2021).

The EPA is responsible for protecting human health and the environment (EPA, FDA, USDA, 2017). Under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), EPA regulates pesticides. Under section 408 of the Federal Food, Drug and Cosmetic Act (FFDCA), EPA establishes the amount of pesticide chemical residues that may be present in food. Under the Toxic Substances Control Act (TSCA) and regulations implementing that statute, EPA currently regulates biotechnology products that are new microorganisms not specifically excluded by the statute (generally those not regulated by other statutes).

The FDA is responsible for protection and promotion of public health (EPA, FDA, USDA, 2017). It regulates under laws including the Food, Drug, and Cosmetic Act (FFDCA), and the Public Health Service Act (PHS), which together, among other things, govern the safety of most foods for humans and animals, including those produced using biotechnology; the safety and effectiveness of intentional genomic alterations in animals produced using biotechnology; and the safety and effectiveness of human and animal drugs and the safety, purity and potency of human biologics, including drugs and human biologics from plants and animals produced using biotechnology.

Within USDA, the Animal and Plant Health Inspection Service (APHIS) is responsible for protecting agriculture from pests and diseases (EPA, FDA, USDA, 2017). Under the Animal Health Protection Act (AHPA) and the Plant Protection Act (PPA), USDA regulates products of biotechnology that may pose a risk to agricultural plant and animal health.

The risks and associated assessments that each agency under the CFRB might consider when looking at gene drive systems for agricultural pests are provided in the figure below. It is important to remember that depending upon the purposes of the gene drive systems for agricultural pests, different laws listed above could be triggered.

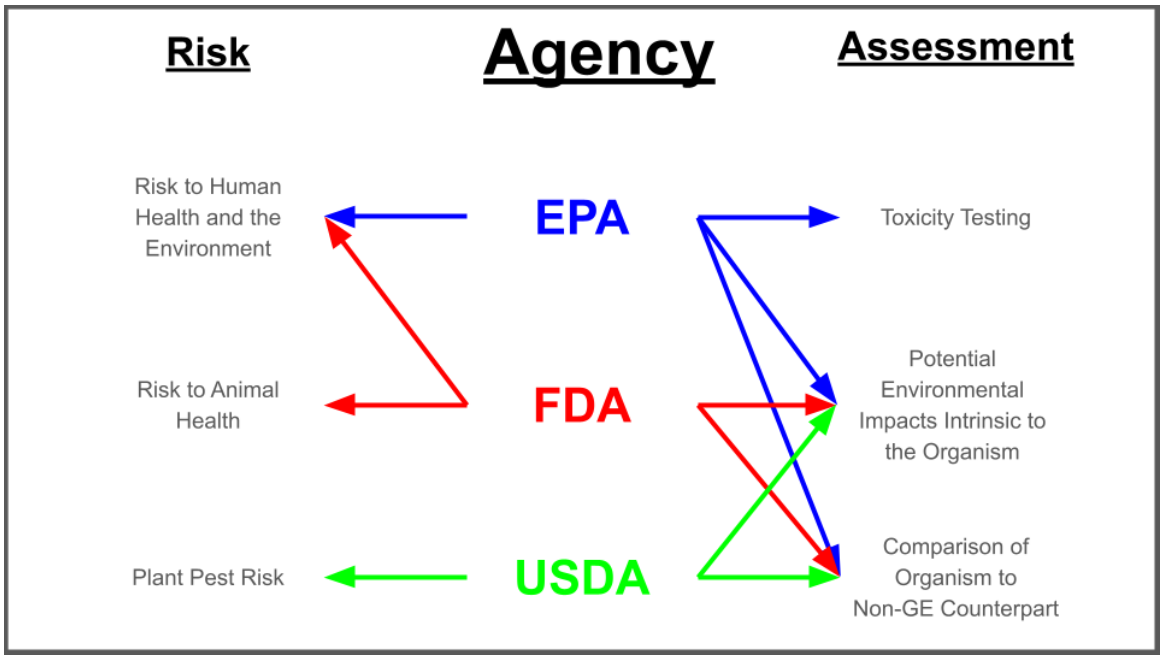

Figure 3 General Overview of Biotechnology Risks and Risk Assessments by Each U.S. Federal Agency. This is an overview of biotechnology regulation for living modified organisms in the U.S. based on information provided by different agency websites. Sources: APHI

As seen in the figure above, different lead agencies will consider different risks and will consider different aspects in their assessments with room for overlap between agencies. Some agencies like the EPA and USDA provide definitions for the risks they consider while the same information could not be found for the FDA. The EPA defines risks to human health or the environment as "the chance of harmful effects to human health or to ecological systems resulting from exposure to an environmental stressor" (EPA, 2022b). While the USDA defines plant pest risks as "The potential for direct or indirect injury to, damage to, or disease in any plant or plant product resulting from introducing or disseminating a plant pest, or the potential for exacerbating the impact of a plant pest" (APHIS, 2021). Current risk assessment language is oriented towards genetically engineered plants, so naming specific methods to assess the risks of gene drive systems for agricultural pests that each agency would use is not available at this time.

While there are still open questions as to how gene drive systems for agricultural pests will be regulated and who precisely will regulate them in the United States, it is the current intention of the federal agencies to regulate gene drive systems for agricultural pests.. For the foreseeable future, one or more agencies of the CFRB will regulate gene drive containing organisms. Given the scope of this paper is limited to gene drives systems in agricultural pests and that the release of a genetically engineered system for plant pests could potentially impact plant health, at a minimum the USDA would likely regulate the release of a gene drive system for an agricultural pest under the authority of the PPA.

5.2 The National Environmental Policy Act and Endangered Species Act

Relevant agencies will also need to consider other statutes like the National Environmental Policy Act (NEPA) and by extension the Endangered Species Act (ESA). While each federal agency may have their own procedures for complying with NEPA, there are three standard outputs when complying with the law: categorical exclusion (CatEx), environmental assessment (EA), or environmental impact statement (EIS) (NEPA, 2022). Initially, agencies are required to produce an EA and depending upon the action may choose to complete an EIS; otherwise, an agency might avoid this requirement through CatEx. An agency can claim that an action should be a CatEx if they can show that the action would not result in a significant effect on the environment. Alternatively, an agency can choose to do an EA if a proposed action is unlikely to have a significant impact or the impacts are unknown. The EA is an exploratory document which provides sufficient evidence and analyses to determine if there is no significant impact of a federal action or if an EIS is required. The EA also analyzes the purpose and need of the federal action as well as plausible alternatives to the proposed federal action. If the EA cannot show a finding of no significant impact an EIS must be done. As part of the EA or EIS process it is common for agencies to also consider impacts to endangered species protected under the ESA.

All federal agencies are subject to NEPA but can have unique interactions with the NEPA Process. The EPA must comply with NEPA but there are certain situations in which EPA actions are excluded from the NEPA process (EPA, 2021). Furthermore, courts have consistently determined that certain EPA processes and environmental reviews are functionally equivalent to NEPA processes (EPA, 2022b). FDA requires applicants to either submit an EA or claim categorical exclusion except in the case of an GE animal defined as an animal drug by the FDA (FDA, 2017). In these cases, the FDA can ignore the NEPA process through determining the animal drug to be safe, which may be a concern for gene drive organisms falling under their jurisdiction (Meghani & Kuzma 2018). The three figures below provide a general overview of the NEPA process for each agency in regard to CatEx, EA, and EIS.

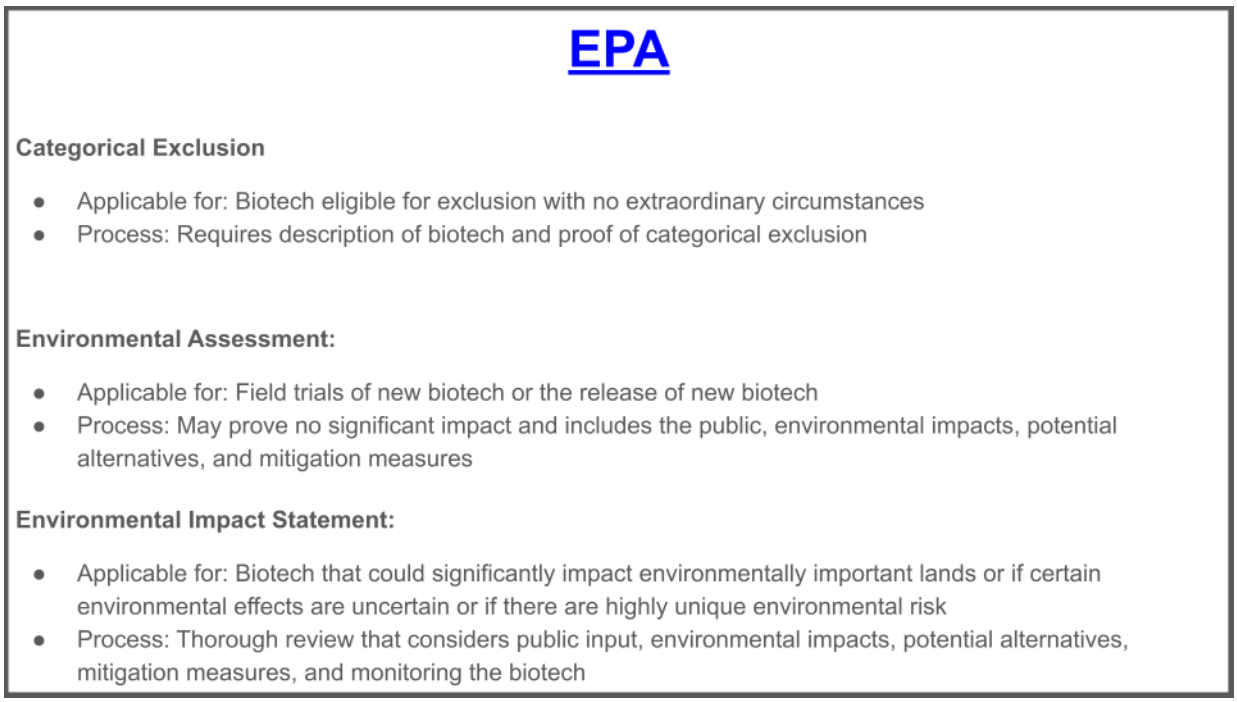

Figure 4 Potential Applications of NEPA under the EPA for Gene Drive Systems for Agricultural Pests. Source: EPA, 2007; EPA 2021.

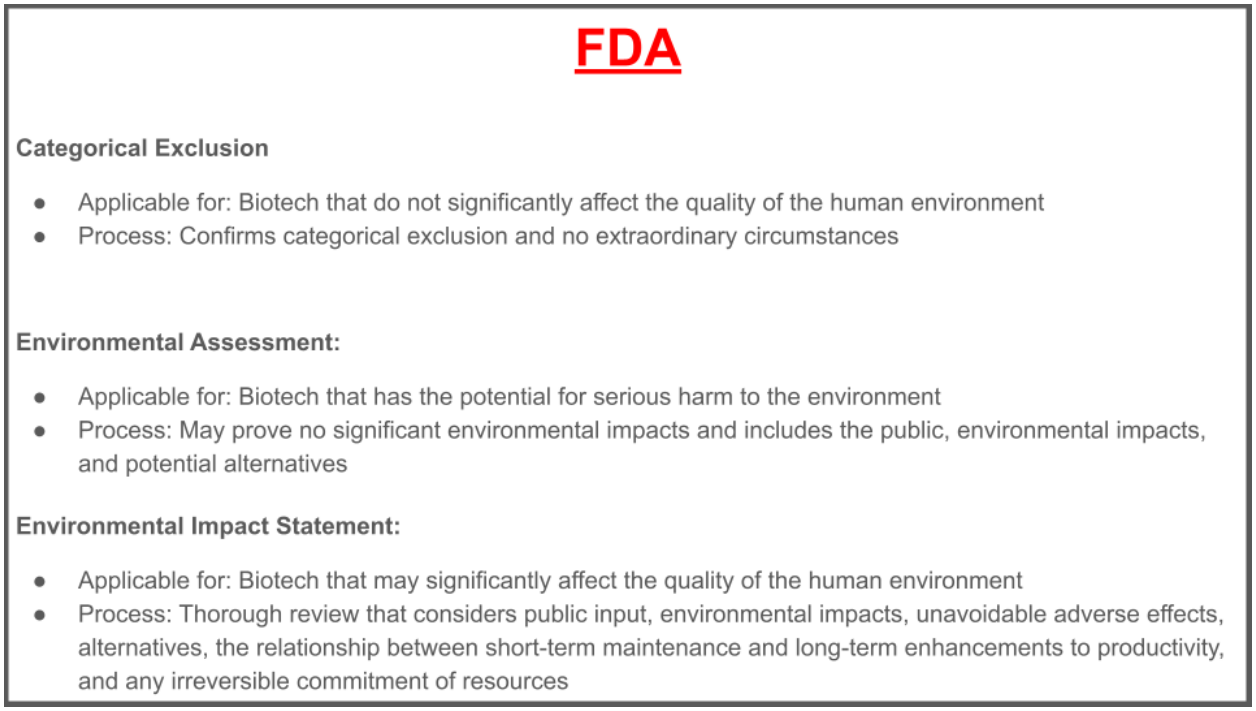

Figure 5 Potential Applications of NEPA under the FDA for Gene Drive Systems for Agricultural Pests. Source: FDA 1997

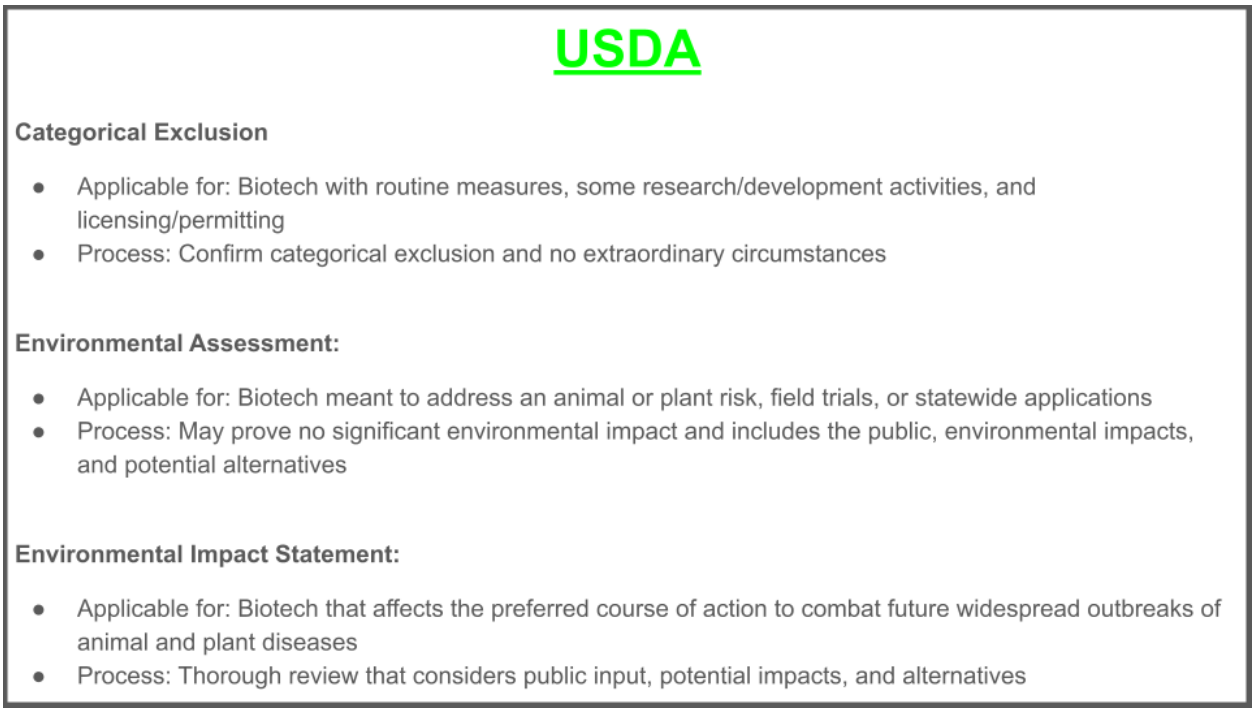

Figure 6 Potential Applications of NEPA under the USDA for Gene Drive Systems for Agricultural Pests. Source: USDA, 1995

Each of these figures summarizes the trigger for either a CatEx, EA, or EIS and the general process each agency goes through based on information provided by each agency. As can be seen across the figures, when doing a CatEx, EA, or EIS each agency carries out relatively the same actions with some slight room for variation. It is important to note that this summary does not fully capture what would be considered in a CatEx, EA, or EIS as these are minimum guidelines that each agency can expand upon.

6.0 Potential Risks Associated with Gene Drive Systems for Managing Agricultural Pests

Through a series of presentations, breakout sessions, and plenary discussions, workshop participants identified six broad categories of risks that should be addressed when considering the potential development and deployment of gene drive pests for agricultural pest management: the biology of target species, the effectiveness of the gene drive, ecological impacts, non-target effects, social dimensions such as public trust and economic considerations, and potential human health impacts. Each is described in turn below.

6.1 Biology of Target Species

To begin, it is useful to consider what consequences gene drives may have on the target organisms themselves. Apart from the obvious consequence of the gene drive affecting a specific phenotype for population suppression, there are also potential outcomes associated with differences in mating preference and mating behavior. There is concern that non gene drive insects of a pest population will not be sexually attracted to gene drive partners and thus completely negate the effectiveness of the drive.

Beyond this, there are concerns that the target organism could somehow become more virulent or aggressive than before because of an unforeseen response to the drive. For instance, there is speculation that with sex-based drives, males could become more aggressive when the sex ratio becomes highly skewed towards males only. Another unfortunate circumstance would be if target organisms developed resistance to a gene drive, either rendering the technology inert, or worse, generating pests that predate on crops at a higher rate or are capable of overcoming other defenses such as pesticides.

The target organism's dispersal needs for a gene drive release are also important for understanding how a gene drive might work in a particular population or species. Release the insects at too low a frequency and they may not spread effectively throughout a population; release them at too high a frequency and they may spread too quickly and not at the desired time. It is for these reasons that developers are working to better understand these components of gene drives.

6.2 Effectiveness of the Gene Drive

An essential risk that was identified by many workshop participants was the risks associated with how gene drives function. Very broadly, these risks involve gene drives not working as designed, such as not spreading in a population as a result of developed insect resistance to the drive. A study released in 2018 by Carrami et al. verified this possibility in *Drosophila melanogaster* using a Cas9 derived homing gene-drive for population suppression. Since homing is reliant on the cutting and insertion of the suppressor gene, non-homologous end-joining increased the mutation rate, which led to the early emergence of resistant alleles (Carrami et al., 2018). This initial component of the study established that simple homing drive designs will not be effective within natural pest populations. Thus, gene drive complexity must be accounted for regarding its influence on risks related to ineffective gene drive and drive resistance. A short-term risk that directly affects an end-user of gene drive technology is that of an ineffective gene drive (e.g., one that does not persist at the level that it was designed for). If a farmer or grower releases a gene drive insect population and the drive does not spread then that translates into lost labor and revenue for the farmer, as well a potential lack of public trust.

Another risk involves the intrinsic nature of the gene drive itself. Altering genetic inheritance via conventional artificial selection affords the advantage of selecting out individuals that are unfit. Gene drive organisms, however, can push any engineered trait through several generations even if it reduces the fitness of the individuals bearing the modification. This inherent property of gene drives may preserve unfit versions of some target species populations in their ecosystems. The ecological effects of preventing natural selection from reducing unfit organisms' populations within ecosystems are currently unknown but it is not unreasonable to worry about potentially destabilizing effects at the community and ecosystem levels. It is also important to consider that although one may succeed in eventually removing gene drive populations from some systems, some of the ecological damage they may have caused may be irreversible.

6.3 Ecological Impacts

Dispersal of the target insect population, described above, may have implications for relationships between target species and other species in a shared ecosystem. Such processes would have possible implications for commensalist/competitive interactions between target and non-target organisms and foreign gene transfer. In instances of insect commensalism, the suppression of a target organism population could affect the survivability of a non-target organism in the same range, especially if a target pest species indirectly benefits non-target species by making food more available. A useful species for demonstrating this is SWD, a potential target organism. This pest consumes the inner flesh of berries before they become ripe, which can cause plants to drop damaged fruit. Ground

dwelling species may then benefit from this accessible food source. If SWD were suppressed via a gene drive, then ground dwelling species would need to rely more on alternative food sources. SWD serves as another illustrative example for considerations of target organism and non-target organism competition. There are two possible outcomes regarding competitor response to SWD removal from an agricultural niche. In one scenario, a competitor pests move in, albeit in a different niche, leaving the SWD niche mostly unoccupied with little to no strain on the growers. In a second scenario, competitor pests are engaged in a pest-species complex with SWD that fully replaces the SWD niche and renews the pest problem, putting severe strain on the growers.

An additional concern is the potential for complete extinction from a region or ecosystem. This could have drastic consequences for other species and the environment. Knock on effects from changing food web dynamics due to the addition or elimination of a species are complex and idiosyncratic and should be considered carefully when discussing gene drive risk.

Participants also raised the possibility that introducing gene drives into an agricultural system could prompt land use changes. Developing controls for specific insects that prey on specific crops may contribute to an exclusive suite of crops being privileged over others because of the ease and cost-effectiveness of their pest management. This would result in decreased crop diversity and, by extension, ecological diversity.

6.4 Non-target Effects

One of the biggest risks posed by the workshop participants were concerns related to possible hybridization of a gene drive insect with that of a closely-related, but non-target species. The ensuing possibility that the gene drive could integrate into the non-target organism is a legitimate concern. This would require the offspring of the hybridization event to be fertile and the events to occur at a high enough rate to meet any threshold required by the gene drive to establish in the population. The actual effects of gene drives persisting or affecting non-target populations will depend on the nature of mating recognition signals of the species involved and should be anticipated.

In contrast to vertical gene transfer (gene flow) through hybridization and outcrossing in a parent-offspring manner, horizontal gene transfer (HGT) is the non-sexual movement of genetic materials between taxonomically distinct organisms (Keeling and Palmer 2008). Although the mechanisms of HGT are not yet well understood, organisms in the environment could generate new traits/functions through HGT to fill new ecological niches. This has been observed amongst bacteria undergoing HGT for the spread of antibiotic resistance genes (Burmeister 2015). In 2021, Xia et al. documented the first case of HGT from a plant to an insect, where the herbivore acquired genetic materials from the host plant to develop resistance to plant defenses. Such a risk is not improbable with gene drive technology as the DNA constructs used fall within the scope of DNA pieces that have been reported to have undergone HGT (Courtier-Orgogozo et al., 2020). The natural organisms that unexpectedly/accidently integrate gene drives or related DNA fragments through HGT from target organisms may alter their own functions and interactions to nature, which could result in significant ecological and/or evolutionary consequences.

The use of pesticides to control key pests in several crops not only kills the target pests but also several potential secondary pests. Thus, decreasing pesticide use was identified as one of the positive outcomes associated with using gene drives for pest management and a key on-boarding factor for public attitudes toward drives (Kokotovich et al., 2022). However, there are possible situations whereby a gene drive may incidentally increase pesticide use. The elimination of one pest may result in the emergence of a secondary pest for which no gene drive is developed (Kokotovich et al., 2022). This will betray the original justification for gene drive use since pesticides will still need to be used for those new pests, resulting in perhaps no significant reduction of pesticide use. A second

outcome would be if a target population develops a resistance to the gene drive under selection pressure, thereby becoming more persistent and aggressive. This too, would require pesticide use and possibly increased spraying.

6.5 Social Dimensions: Stakeholders, Public Audiences, and Economic Considerations

Another important set of risks of this technology involves public trust in regulatory systems. Participants noted that the regulatory system in the U.S. is currently ill prepared to regulate gene drive technologies. For example, it has been recommended that public engagement should play a prominent role in potential gene drive uses (NASEM, 2016; Long et al., 2020). Nevertheless, the current mechanisms of public engagement at the regulatory level in the U.S. are not able to incorporate public engagement recommendations proposed by gene drive developers and academics (West et al., 2022). Thus, releasing gene drive organisms before regulatory systems are modified to be ready to incorporate expert recommendations when it comes to public engagement, may seriously harm public trust in gene drive governance.

Another dimension of trust is growers may lose faith in gene drives if the drive does not function well enough to resolve their problem. This will negatively impact the adoption of gene drives by these end-users in the future. This places immense pressure on gene drive developers to develop safe and effective systems that function as desired. Other possible barriers to grower/farmer adoption of this technology apart from cost or a malfunctioning drive might include a lack of understanding/ignorance of the technology, a fear of the technology, or an unwillingness to adopt a new system. It is important to recognize that growers and farmers will make decisions about gene drive use within the context of those tools that are already available to them.

Other risks and tensions referenced during the course of the workshop included how gene drive technology might influence the decisions and profits of growers, farmers, and consumers. This is an important point of consideration because these are the stakeholders who will ultimately be using this technology. Grower profits were brought up many times during the workshop. Though it is reasonable to anticipate that gene drives could save a farmer money because it will reduce the need/cost of other pest management materials and labor, there are instances where this may not be the case. Firstly, what would be the initial cost to the grower to adopt this technology? There is of course the cost of purchasing the gene drive insects, but then there could also be costs associated with governmental permits, changes to grower infrastructure to facilitate gene drive release, and the time taken to train and learn about this technology. If implementing gene drive into their pest management practices is perceived as too much of a hassle (e.g., includes challenges associated with consumer perceptions of gene drives in agriculture and marketing issues) and too costly, then we risk innovating and investing in a technology that does not become widely adopted.

Another social dimension that participants described was akin to a moral hazard stemming from the ways in which a particular gene drive is designed and deployed. For example, if gene drives are ever designed to revert pesticide resistance, or if gene drives are designed to protect pollinators or vulnerable target species for example, then pesticide use may actually increase rather than decrease in some contexts. Unlike the case of gene drive use for malaria control, in which the goal is to save human lives, the motivations and values involved in gene drive use for agricultural purposes will likely result in the development of business models that may allow profitable uses for gene drives. For example, gene drive could in theory be used to revert insecticide resistance allowing pesticide companies to resell products that were discontinued due to the development of resistance in their target pests. Similarly, gene drives could be used to protect pollinators and key natural enemies lending themselves to potentially profitable business models that could market pesticides as friendly to genetically engineered pollinators and natural enemies. Gene drives could ultimately act as techno fixes that may prevent investment in solving the root causes of unsustainable pest control practices,

preserving unfair and unsustainable practices, and increasing externalities. On the other hand, if gene drive is deemed as an acceptable tool in the integrated pest management (IPM) arsenal, and if industry used it as part of profitable pest control solutions, it is fair to consider corporations as relevant stakeholders. If that becomes the case, risk assessments regarding gene drive use for agricultural applications are likely to conceptualize loss of profits, lack of public acceptance and reduced market-share as harms worthy of risk assessments. In these scenarios, risk assessments conducted by corporations may fundamentally differ from what academics have so far considered appropriate endpoints in risk assessments of gene drives designed to protect public health or the environment.

6.6 Potential Impacts on Human Health

Workshop participants identified broad potential risks to human health or potential *perceived* risks of gene drive systems as an agricultural pest management tool. Participants noted that direct and indirect adverse effects to human health may be potential risks as are how these potential risks accumulate over time. Pervasive potential uncertainties may also have unforeseen impacts on potential human health risks.

7.0 Data Needs

On the second day of the workshop, the participants identified research priorities for the future, categorized as near-, medium- and long-term data needs. Near-term was defined as within the next five years; medium-term as the next five to fifteen years; and long-term as greater than fifteen years into the future. The outcomes of the proposed areas of research should fill knowledge gaps and inform decision-making related to regulation, oversight and research funding. After workshop participants identified potential risks of using gene drive to manage agricultural pests, they were split into breakout sessions to both identify key data requirements for completing a risk assessment and to categorize those data by short (> 5 years), medium (5-15 years), and long-term needs (>15 years).

7.1 Biology of Target Species

Short-term data needs (< 5 years)

Participants suggest that much of the data that should be collected in the short term are about the biology of the target organism. Better understanding of the biology of the organism should, according to workshop participants, begin with defining the target organism with great clarity, essentially asking, where does the target organism "stop" compared to closely related populations. To that end, understanding the close proximity of related populations, assortative mating, population genomics of related and surrounding species, and isolated subpopulations may help identify genetic variants that may isolate the impact of the gene drive. In short, participants want to understand the target organism population throughout its geographic range.

Additionally, participants also identified a number of molecular level data needs. Basic understanding of the genomics of the target species is critical. Participants also pointed to the importance of understanding the population genetics and genomics of the wild populations. Participants also want to understand the impact of different genetic backgrounds on gene drive mechanisms.

Finally, workshop participants also identified data needs in the context of the target organism in its environment. One basic biology data need includes understanding the lifespan of the target organism. Participants also noted that understanding dispersal patterns of the target organism would help predict how a gene drive would move through a given population. Additional behavioral dimensions are needed, including mating biologies such as assortative mating phenotypes and male

mating competitiveness function in the environment. Participants also want to understand if the target organism behaves differently in different environments. Finally, participants want to identify the fitness costs to the target organisms.

7.2 Effectiveness of the Gene Drive

Short-term data needs (< 5 years)

In short, one of the driving questions for workshop participants with respect to gene drive efficacy is quite simply: is it feasible? One tool for understanding potential feasibility from an efficacy perspective is to better understand the persistence of naturally occurring gene drives, with particular attention to how often breakage occurs.

Some participants also indicate that researchers should identify findings that might lead to total cessation of the project's development, both in terms of risk and in terms of efficacy.

Workshop participants put forth a set of data needs that is relevant to both the effectiveness of the gene drive and to ecological impacts: the importance of understanding the stability of the gene drive and how specifically the gene drive stays within target species. Additionally, participants argue that understanding the population genetics of the wild populations would help to predict efficacy and background level of resistance, as well as variability in gene drive. Relatedly, participants want to understand the formation of resistant mutations that may occur during mass rearing of the target organism.

Participants also want to understand how gene drives perform in different environments. They also want to understand density dependence from an efficacy perspective because survival changes when you change the density. Relatedly, other participants want to understand the drive threshold of the target organism.

Medium-term data needs (5-15 years)

Once multiple generations of a laboratory-based gene drive have been produced, participants noted that one important biological issue is understanding the genetic variation in the target organism.

While mentioned in the short-term data needs, participants also suggested that the exploration of what scale is necessary for a gene drive system to work should also take place over time, at least through the medium term. This is because understanding the scale would necessitate a range of disciplinary data, some of which includes geographic scale and the economic cost/benefit ratio depending on that land scale.

Additionally, participants want to continue modeling the efficacy of gene drive applications, particularly as additional data come in that can revise model parameters and assumptions.

Long-term data needs (>15 years)

Broadly, participants noted the importance of understanding the implications of both successful and unsuccessful gene drive dispersal. Additionally, workshop participants identified the need to understand potential evolution of resistance to gene drive systems, which would limit the spread and therefore efficacy of the gene drive. Workshop participants therefore called for research to be conducted about the means by which resistance might evolve in populations.

7.3 Ecological Impacts

Short-term data needs (< 5 years)

Participants identified a number of ecological issues that are critical for understanding how gene drive systems function in the environment, yet many of those issues need to be understood over time. One set of data needs that can be explored in the short term, however, is identifying what non-target organisms have a close relationship with the target organism.

Modeling can also provide important information in the short-term, assuming the data requirements for setting model parameters are available or can be collected relatively quickly. One of the most important ecological questions that participants want to understand is what happens when there are temporarily more pests in the environment, as would be the case when gene drive organisms are dispersed.

Additionally, participants want to understand potential impacts on target species outside of the intended management area. In other words, participants want to understand dispersal from a biosafety perspective: how does the target organism move outside of the target area? How likely would it be that the modified organism gets to an area where it is not wanted, like its native range or center of origin? This is another arena where modeling would be a way to understand these questions without adding unnecessary risk to ecosystems. To mitigate risk to ecosystems for which the gene drive is not intended, participants want to understand the best tools for establishing containment by designing drives with limitations to prevent uncontrolled spread or possible target species extinction. Participants also want to establish clear containment strategies for field trials, be they physical or biochemical, to prevent unintended consequences.

Medium-term data needs (5-15 years)

Importantly, participants note that data collection about ecological impacts of gene drive systems is important across all three stages of data needs and that studying ecological effects over time is critical for understanding impacts of gene drive organisms. For example, participants noted that if successful, a gene drive will likely leave an unfilled niche that will fill with another species or secondary pest. In other words, participants call for longer-term understanding of wider community interactions where the gene drive has eradicated or extirpated the target pest.

Other participants wanted to interrogate these same questions but focused on the role of modeling to explore these issues, even in the short term. In particular, with respect to ecological impacts participants want to model spread, face, and effects. Of course, field experiments and modeling are not mutually exclusive and field experiments can be one way to test model assumptions, focus on specific sites, and understand sensitivity of different parameters. In general, participants highlight the importance of modeling as a tool for understanding and making decisions about the complexity of the systems in which gene drive may be deployed.

Long-term data needs (>15 years)

Workshop participants called for ongoing data collection regarding impacts on broader landscape ecologies where gene drive organisms might be released. One key long-term data need for ecosystem function that participants identified is developing a research agenda around understanding longer-term ecological changes in the field. To that end, participants also noted the importance of continuing to collect data about changes in species interactions over time, in particular predator-prey relationships, as well as non-target organisms where the target pest has been eradicated.

Another ecological dimension that participants wanted to explore is the impact on target species outside the treatment area. Participants pointed out that while there was some discussion about

rare and catastrophic events—such as global extinction of target species or localized population explosions with deleterious impacts on local environments—there is little understanding about how to interrogate these issues even empirically. As such, workshop participants posited that relevant research agendas might be developed over a longer time period so that such events could be identified, and researchers could collaborate on developing techniques for investigating rare and catastrophic events.

7.4 Non-target Effects

Workshop participants wanted to address both vertical and horizontal non-target effects across multiple time scales. As such, they called for ongoing modeling and field investigations into the potential for impacting non-target species through gene transfer. Participants want to see investigations into two distinct gene transfer pathways: one, vertically through hybridization with related populations and two, horizontally through trophic levels. As such, workshop participants also want to see investigations into potential toxicity to the target organism's predators and throughout the trophic levels, with particular concern for vertebrates.

7.5 Social Dimensions: Stakeholders, Public Audiences, and Economic Considerations

Short-term data needs (< 5 years)

Workshop participants identified four broad categories of social dimensions that they want to see investigated in the short-term: stakeholder perceptions, governance economic considerations, and broader societal perceptions.

Participants want to see stakeholders engaged to have a better understanding of the interests and values that underpin stakeholder perspectives. From a practical perspective, participants want to see data on likelihood of stakeholder adoption, how a gene drive might fit into existing pest management tools, and how knowledge of other pest management tools impacts these perspectives. Additionally, participants want to see stakeholders engaged to help identify and prioritize potential risks.

Understanding risk, participants point out, is also situated in the broader risk frameworks that already exist within the existing regulatory framework. As such, participants want to see research conducted on (1) identifying the regulatory steps that will be required to use a gene drive system for agricultural pest management and (2) the existing risk framework and how they handle hazard identification for gene drive. And finally, as a critical piece of governance, participants want to see a mechanism for updating shared knowledge, space for iteration, and pathways for allowing that shared knowledge to shape policy and management of gene drive.

From the economic perspective, participants identified the importance of understanding the opportunity cost of using a gene drive system. To that end, they were interested in understanding the risk of using existing control methods versus the value of a gene drive. Participants are also interested in how growers make sense of the trade-offs with other forms of pest control. And finally, participants are curious to know how the scale of operation might influence perception of gene drive for pest management.

Finally, participants want to understand broader societal perceptions about gene drive. While a range of participants highlighted the importance of engaging broader public audiences to understand their perception of gene drive, the nature and timing of that engagement is subject to some debate. In addition to exploring broader public perceptions, participants want to explore perceptions of gene drive from different cultural frameworks.

Medium-term data needs (5-15 years)

Again, participants noted that engaging stakeholders and public audiences should be ongoing activities. Engaging stakeholders to identify and prioritize risks, and including stakeholders in all aspects of risk assessment, is one set of issues that should be addressed in the short-, medium-, and long-term data collection frameworks. Moreover, participants suggest that the risk framework that is ultimately used should incorporate modeling components to provide more nuanced decision support tools.

Another issue that participants suggest studying over short and medium term is empirically studying perceptions of genetic pest management across different cultural frameworks. Understanding perspectives across cultures would help developers and decision makers better understand local contexts for potential gene drive applications. Participants suggested that the modeling efforts that have been called for elsewhere in this report should integrate stakeholder concerns and needs so that the engagement and processes alike can be iterative.

Participants also identified a number of economic dimensions that they thought would be most effective to investigate in the medium term. For example, participants suggested that this would be a good time to engage trading partners into conversations about the implications of using gene drive for pest management of different crops. Additionally, participants noted that this would also be a good time to evaluate the opportunity cost of conducting gene drive field trials.

Long-term Data Needs (>15 years)

As noted elsewhere in this report, stakeholder engagement should be included in all aspects of risk assessment and throughout monitoring phases of gene drive releases. Developing a clear and context-specific—but also flexible—engagement plan for the long-term will be important for this dimension as a mechanism for updating knowledge and societal perspectives. Ongoing stakeholder engagement may be one effective way to address uncertainties that characterize gene drive releases.

Additionally, workshop participants suggest developing a research agenda around policy and governance frameworks. One, participants suggest researching and clarifying the regulatory steps that will be required for gene drive organisms to be released into the environment. Two, participants want to explore the potential for better incorporating inclusion of societal issues into the existing risk assessment framework that governs biotechnology.

7.6 Potential Harm to Human Health

Interestingly, while human health was noted as a potential risk—or at least the perception of human health risks—the breakout groups did not include human health data needs in their prioritization. Perhaps this gap is because most scientists do not perceive human health concerns to be of particular risk in the context of agricultural biotechnology. Regardless, attention to risk perception around human health and genetic modifications has been attended to elsewhere in the literature (cite).

8.0 Conclusions and Next Steps

In short, this workshop brought together a range of stakeholder perspectives to identify needs for risk assessments of gene drives used in agriculture based on current knowledge. This workshop also more broadly conceptualized risk assessment in the face of the uncertainties that characterize gene drive research and development. Biological characterization, ecological and non-target impacts,

and social dimensions represent key factors that should form the basis of gene drive research agendas. Each of these—and others—will need to be considered over time. This longitudinal approach to research can be challenging for traditional funding cycles, and therefore one next step is to identify potential frameworks, tools, and resources for developing and maintaining long-term data collection needs related to gene drive risk assessment research programs.

The breadth of potential risks that participants raised point to the need of (1) the critical need for continuing this discourse with both the experts that attended and with broader stakeholder groups, and (2) the importance of interdisciplinarity around the potential use of gene drive as a management tool for agricultural pests. Moving forward, we hope that this workshop sparks professional relationships that spurs interdisciplinary collaboration. As modeling is a key tool for understanding the behaviors of gene drives in agricultural pests, one of the key takeaways is the need to integrate social science data into the models that researchers across government and academia alike are producing. To that end, one important issue that was not fully articulated at this workshop was what kinds of social science data might be needed for such an endeavor, or even what kinds of social science data could even be produced to support this effort.

Finally, virtual workshops such as this one open up access to broader stakeholders than might otherwise be able to attend and contribute. It is our hope that, as we return our attention to increasing openness and in-person events, we hold true to the goals of inclusion and accessibility of participating in interdisciplinary and cross-sector collaborations.

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