NExTRAC Gene Drives in Biomedical Research Working Group

Cinnamon Bloss, PhD

Zach Adelman, PhD

NExTRAC Meeting – June 25, 2021

Charge to NExTRAC

In December 2019, Dr. Francis Collins charged the NExTRAC and announced that NIH would convene a Working Group of the NExTRAC to:

- Assist in the development of a path forward for biomedical research involving gene drive modified organisms

Gene Drives in Biomedical Research Working Group

Charged to:

- Consider whether existing biosafety guidance is adequate for contained laboratory research utilizing gene drive technology

- Outline conditions (if any) under which NIH could consider supporting field release of gene drive-modified organisms

Gene Drives in Biomedical Research Working Group

Provide advice on the following issues:

- Given the diverse applications and species that may be used in gene drive research with different risks, is the current landscape of biosafety guidance adequate for contained research?

- What knowledge and conditions should be in place to help ensure that field release research of gene drive modified organisms could be conducted safely and ethically?

Working Group Roster

Co-Chairs

- Adelman, Zach (Texas A&M University)
- Bloss, Cinnamon (University of California, San Diego)

Members

- Boris-Lawrie, Kathleen (University of Minnesota)
- Lee, Benhur (Icahn School of Medicine at Mount Sinai)
- Lee, Dean (Nationwide Children’s Hospital, Ohio State University)
- Oye, Ken (Massachusetts Institute of Technology)
- Porteus, Matthew (Stanford University)

Ad hoc Members

- Collins, James (Arizona State University)
- Delborne, Jason (North Carolina State University)
- Hall, Lee (NIH)
- Heitman, Elizabeth (University of Texas Southwestern Medical Center)

Process of Deliberation

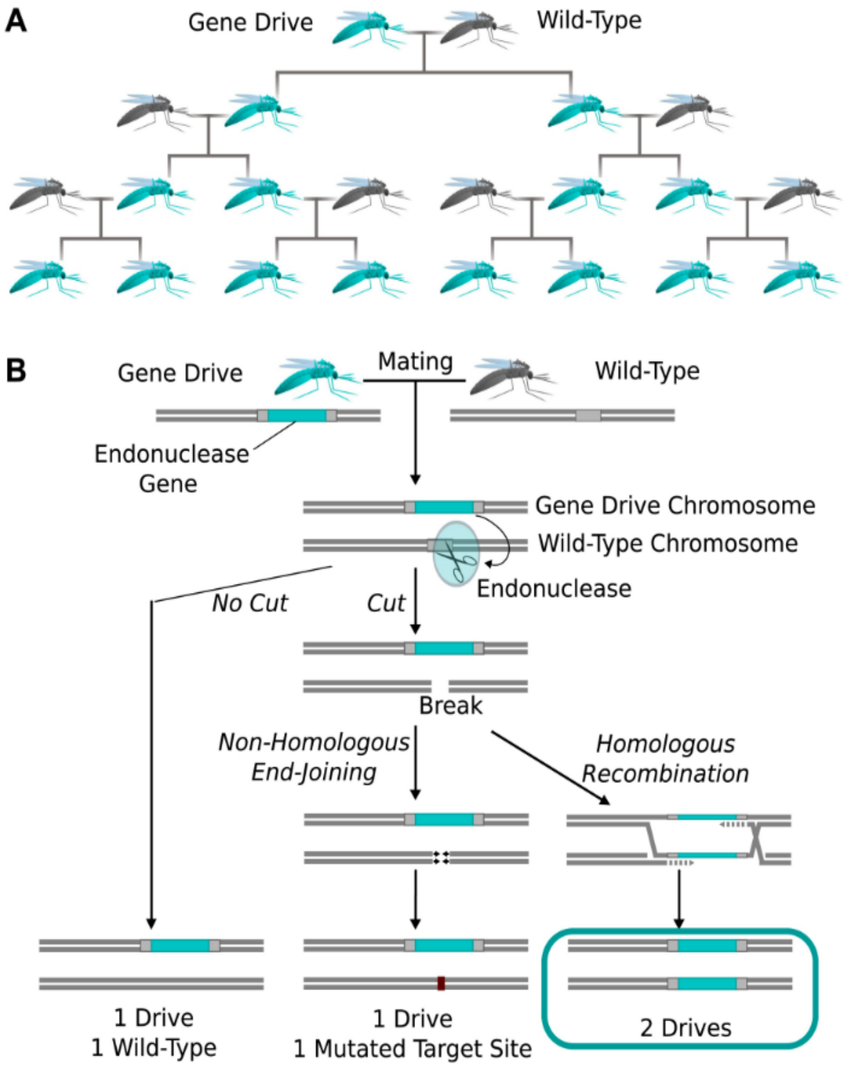
Bimonthly working group meetings

Presentations by experts

Public Gene Drive Workshop

Topics for Deliberation

- Current state of gene drive technologies
- Adequacy of biosafety guidance for contained research
- Biological and environmental risk mitigation strategies
- Risk/benefit assessment
- Stakeholder engagement



NExTRAC Gene Drive Workshop
November 9-10, 2020

11/6/2020

NATIONAL INSTITUTES OF HEALTH

Novel and Exceptional Technology and Research Advisory Committee (NExTRAC)

NIH National Institutes of Health

Virtual Meeting
November 9-10, 2020 (All times EST)

AGENDA – Day 1

10:00 AM – 10:15 AM **Welcome**
Carrie Wolinetz, PhD and Richard Whitley, MD

NEXTRAC WORKSHOP
GENE DRIVES: BIOSAFETY GUIDANCE AND CONDITIONS FOR FIELD RELEASE RESEARCH

SESSION I: GENE DRIVES IN BIOMEDICAL RESEARCH
The charge to the Gene Drives in Biomedical Research Working Group will be presented, along with an overview of gene drive technologies and their applications.

10:15 AM – 10:30 AM **Overview of Charge to the Gene Drives in Biomedical Research Working Group**

Gene Drives Working Group Co-Chairs:
Zach Adelman, PhD and Cinnamon Bloss, PhD

10:30 AM – 11:00 AM **Overview of Gene Drive Technologies and Applications**
Anthony James, PhD

SESSION II: BIOSAFETY GUIDANCE FOR CONTAINED RESEARCH
Discuss existing landscape of biosafety guidance and examine what, if any, barriers exist for applying such guidance to contained gene drive research, and whether additional guidance would be useful.

11:00 AM – 12:30 PM **Panel Discussion**
Moderator: Zach Adelman, PhD

Panelists:
1. Kathryn Harris, PhD RBP
2. Lyric Bartholomay, PhD
3. David Gillum, MS RBP
4. Ruth Müller, PhD

- *Is current physical containment guidance adequate to address contained research with organisms containing gene drives?*
- *Would additional physical containment guidance for certain species*

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Webcast Archive:
https://osp.od.nih.gov/biotechnology/main-nextrac/#meetings

Gene Drives in Biomedical Research Working Group Report

Organization of Report

Charge Part 1. Consider whether existing biosafety guidance is adequate for contained laboratory research utilizing gene drive technology

Charge Part 2. Outline conditions (if any) under which NIH could consider supporting field release of gene drive modified organisms

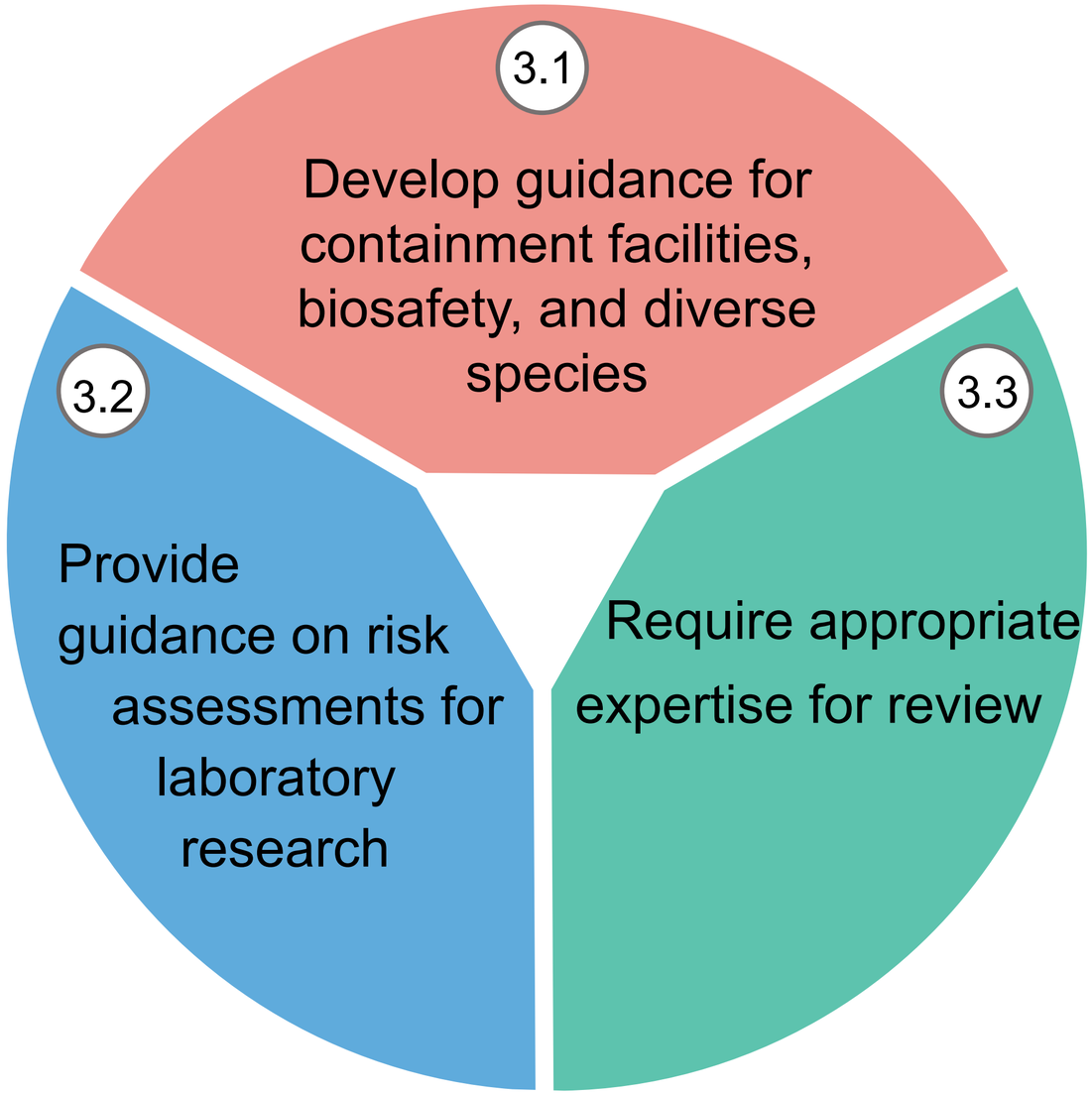
Section III. Biosafety Guidance for Contained Research

Section IV. Biological and Environmental Risk Mitigation Approaches

Section V. Strategies for Risk/Benefit Assessments for Field Release of Gene Drive Modified Organisms

Section VI. Strategies for Stakeholder Engagement Regarding Gene Drive Modified Organisms

Recommendations for Biosafety Guidance for Contained Research



Biosafety Guidance for Contained Research

Working Group Considerations

U.S. biosafety guidance does not specifically address gene drive research in contained laboratory settings

Containment conditions not available or widely adopted for many species likely to be used in gene drive research

Working Group Recommendation 3.1

Develop guidance for:

- Uniform standards for design and construction of containment facilities
- Biosafety considerations for work practices
- The diverse species that could be used in gene drive research

Biosafety Guidance for Contained Research

Working Group Considerations

Current guidance does not consider recombinant or synthetic nucleic acid molecules that have potential to spread/persist in the environment - presenting different/increased risks as compared to manipulations unlikely to do so

Need to identify what scientific questions need to be asked and what data are needed to facilitate laboratory risk assessment

Working Group Recommendation 3.2

Provide guidance on the considerations for risk assessments for laboratory gene drive research to assist investigators, BSOs, and IBCs in determining appropriate conditions for contained research (e.g., dealing with complexity, uncertainty, and context)

Biosafety Guidance for Contained Research

Working Group Considerations

Assessment of potential risks to the environment posed by the escape of gene drive modified organisms is an aspect not typically undertaken by IBCs

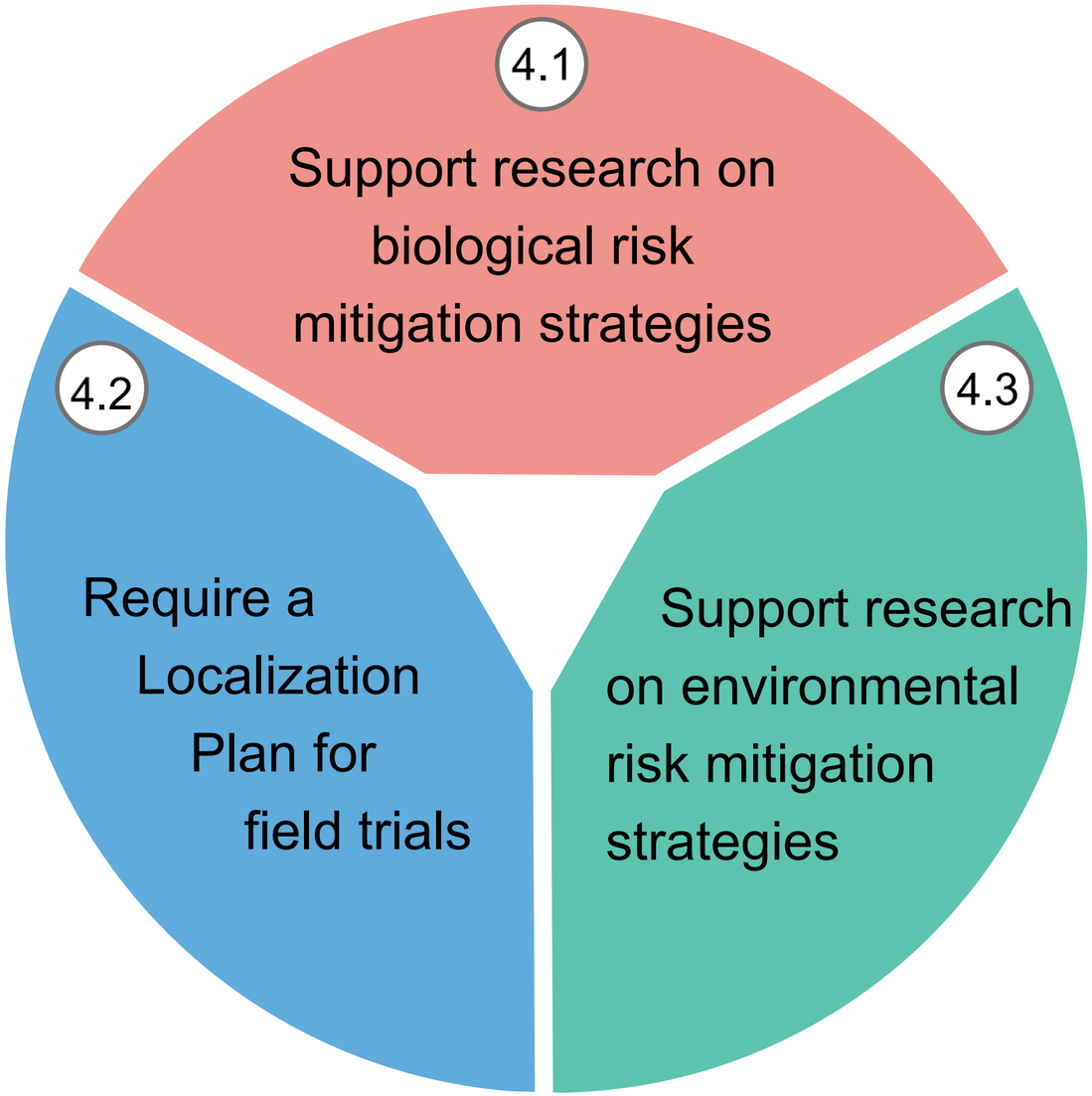
Inspections of facilities housing gene drive modified organisms are critical to ensure containment standards are rigorously followed

Working Group Recommendation 3.3

Require appropriate expertise in the review of gene drive research:

- Develop guidance on specific IBC expertise needed for review of gene drive research (e.g., entomology, ecology, evolutionary biology)
- Require a BSO be appointed to the IBC when conducting experiments with gene drive modified organisms capable of spreading in the environment

Recommendations for Biological and Environmental Risk Mitigation Approaches



Biological and Environmental Risk Mitigation Approaches

Working Group Considerations	Working Group Recommendation 4.1
Biological risk mitigation strategies are at the theoretical or early proof-of-concept stages and require additional research to provide evidence of effectiveness before use as potential safeguards in both laboratory and field release studies It is challenging to evaluate approaches for risk mitigation strategies separately from studies focused on the development of the gene drive technology itself	Support research on biological risk mitigation strategies, including the identification of critical areas of uncertainty and approaches to mitigate them

Biological and Environmental Risk Mitigation Approaches

Working Group Considerations

Experimental designs that are confinable and/or reversible should exhibit a more clearly defined risk profile than approaches with the potential to spread more widely

The ability to constrain the spread of a gene drive depends on specific molecular architecture, target organisms, conditions of release, local environments, availability of mitigation approaches and social contexts

Working Group Recommendation 4.2

Require the Approach section of the NIH application or proposal to include a Localization Plan for field trials (which articulates how the gene drive is proposed to be confined/reversed)

Biological and Environmental Risk Mitigation Approaches

Working Group Considerations

An understanding of likely ecological and evolutionary interactions is necessary to inform appropriate risk mitigation strategies

Perspectives of local communities and indigenous knowledge are critical to understanding the environmental risk profile for specific locations

Working Group Recommendation 4.3

Support research on environmental risk mitigation strategies based on evaluation of potential impact on eco-evolutionary dynamics and informed by stakeholder engagement

Recommendations for Risk/Benefit Assessments for Field Release of Gene Drive Modified Organisms

NIH should require all requests for support of field trials involving gene drives to…

Risk/Benefit Assessments for Field Release of Gene Drive Modified Organisms

Working Group Considerations

Balancing potential benefits/harms

Comparing with existing interventions

Dealing with ecological and evolutionary complexity

Considering potential social and ethical benefits/harms

Working Group Recommendation 5.1

Require the Approach section of the NIH application or proposal to include a risk/benefit assessment plan addressing potential benefits and potential harms to populations and environments

Risk/Benefit Assessments for Field Release of Gene Drive Modified Organisms

Working Group Considerations

2016 NASEM report

As research progresses from laboratory to field release, the data accrued from each phase should feed into the risk/benefit assessment

What will be the impact of the research if field release ultimately does not occur

Working Group Recommendation 5.2

Require the Approach section of the NIH application or proposal to include phased research plans with activities designed to proceed from lower to higher risk

Risk/Benefit Assessments for Field Release of Gene Drive Modified Organisms

Working Group Considerations

Iterative risk/benefit assessments are needed to inform:

- Decision to move to the next phase of research
- Whether modifications are needed to the research plan

Decision to move to the next phase will vary with the context of particular research projects, locations, and communities

Working Group Recommendation 5.3

Require the Approach section of the NIH application or proposal to include milestones for decisions regarding whether to proceed to the next phase

Risk/Benefit Assessments for Field Release of Gene Drive Modified Organisms

Working Group Considerations

U.S. regulatory processes for evaluating gene drive technology are limited in how and what information is shared with communities/publics and how input from these groups is used in decision-making

Independent evaluation is key to building trust essential to any potential field trial

Working Group Recommendation 5.4

Utilize an independent board to provide input on assessments of potential benefits/harms, milestones, and any associated recommendations

Risk/Benefit Assessments for Field Release of Gene Drive Modified Organisms

Working Group Considerations

NIH's role in supporting research of risk/benefits assessments to prevent disease and improve human health

- Stewardship and promoting safe, responsible, conduct of research

Transparency in decision making is vital to promoting public trust and engagement

Working Group Recommendation 5.5

Make risk/benefit assessments and any associated recommendations from the independent board publicly available

Recommendations for Strategies for Stakeholder Engagement

Strategies for Stakeholder Engagement

Working Group Considerations

Effective stakeholder and community engagement

- Consider interests, values, goals, and perspectives of stakeholders to promote public trust
- Establish support/funding mechanisms for project planning and early engagement

Working Group Recommendation 6.1

Support planning projects to identify potential trial sites and associated stakeholders and conduct preliminary engagement activities that could inform future trials

Strategies for Stakeholder Engagement

Working Group Considerations

Stakeholder engagement plans should address:

- Identification of affected groups
- Strategies for engagement
- Balancing maximal inclusivity with prioritization of those most directly affected
- Incorporation and consideration of input

Working Group Recommendation 6.2

Require the Approach section of the NIH application or proposal to include a plan for stakeholder engagement that articulates who will perform engagement activities, and how input would be incorporated into decisions about experimental design and whether to proceed through the phases of the research plan

Strategies for Stakeholder Engagement

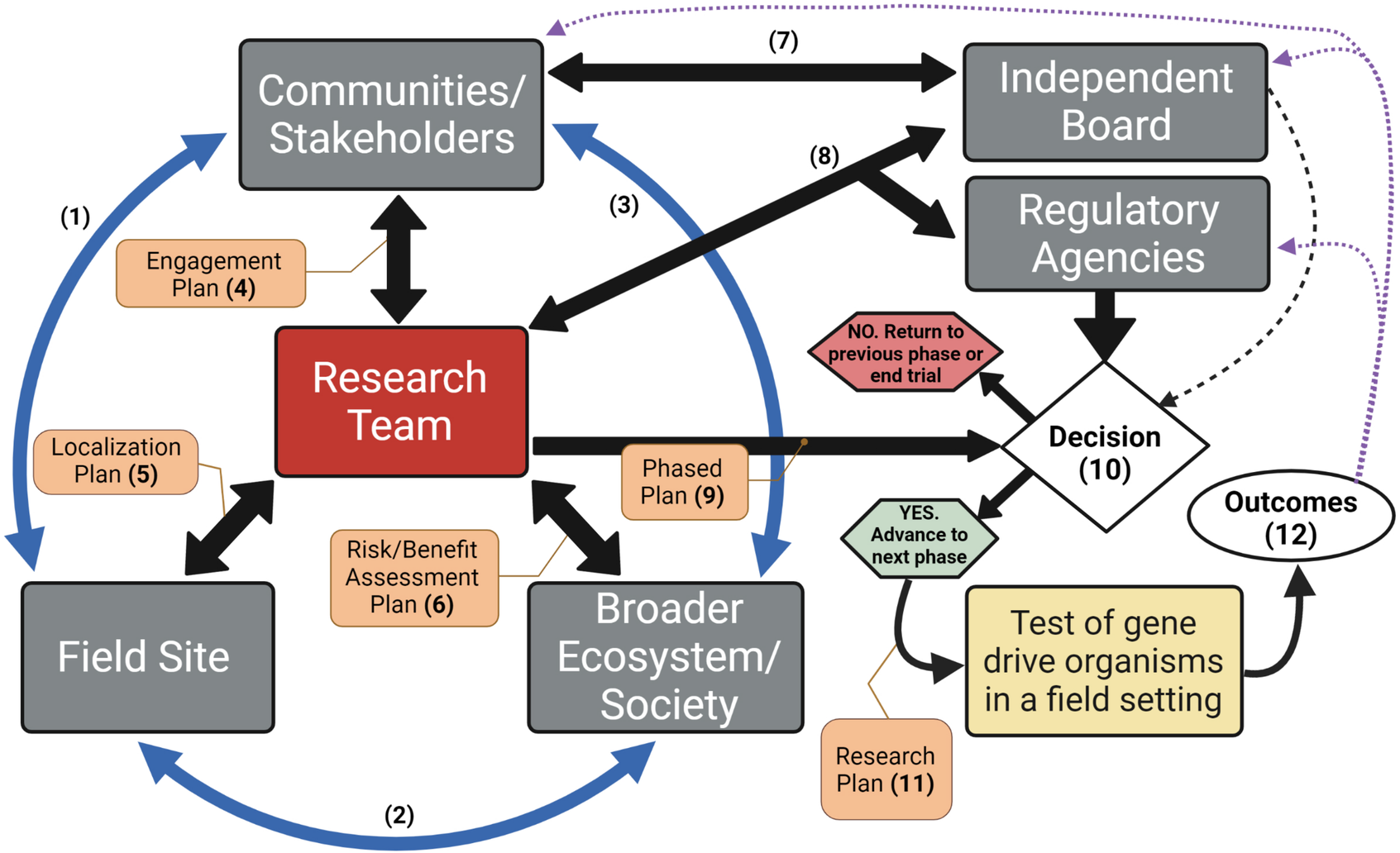
Working Group Considerations

Evaluating effectiveness of engagement

Research to establish best practices

Working Group Recommendation 6.3

Support research on establishing best practices for stakeholder engagement for laboratory or field-based gene drive research


Communities/ Stakeholders
(7)
Independent Board
(8)
Regulatory Agencies
(1)
(3)
Engagement Plan (4)
Research Team
NO. Return to previous phase or end trial
Decision (10)
Localization Plan (5)
Phased Plan (9)
YES. Advance to next phase
Outcomes (12)
Risk/Benefit Assessment Plan (6)
Field Site
Broader Ecosystem/ Society
Test of gene drive organisms in a field setting
Research Plan (11)
(2)