Biosafety Guidance for Contained Research with Gene Drive Modified Organisms—A Biosafety Officer's Perspective

David Gillum, MS, RBP
2020 President of ABSA International
ASU Chief Safety Officer
https://www.linkedin.com/in/davegillum/

This presentation will briefly review 3 topics

1. Roles in assessing gene drive research

   Biosafety Officers—BSOs

   Institutional Biosafety Committees—IBCs

2. Need to augment existing biosafety guidance

3. Next steps—Policy considerations, training and outreach

Safeguarding gene drive experiments in the lab

Akbari, Omar S., et al. "Safeguarding gene drive experiments in the laboratory." *Science* 349.6251 (2015): 927-929.

Type	Stringent Confinement Strategy	Risk Assessment (Example Questions)
Molecular	Separate components required for genetic drive; Target synthetic sequences absent from wild organisms.	How do you assess the different molecular confinement strategies? How do you demonstrate a particular strategy is better than another? How does natural evolution or mutation factor in?
Ecological	Perform experiments outside the habitable range of the organism; Perform experiments in areas without potential wild mates.	What about locations with seasons where a species could live? How far away from a habitable range? With climate change, species are rapidly moving, so how do you really know?
Reproductive	Use a laboratory strain that cannot reproduce with wild organisms.	How do you determine which strategies are best for each species? How do you demonstrate the strategy will work?
Barrier	Physical barriers between organisms and the environment; Remove barriers only when organisms are inactive; Impose environmental constraints; Take precautions to minimize breaches due to human error.	How different is this than **physical containment** strategies typically employed in traditional biosafety?

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BSOs, IBCs and Understanding Gene Drives

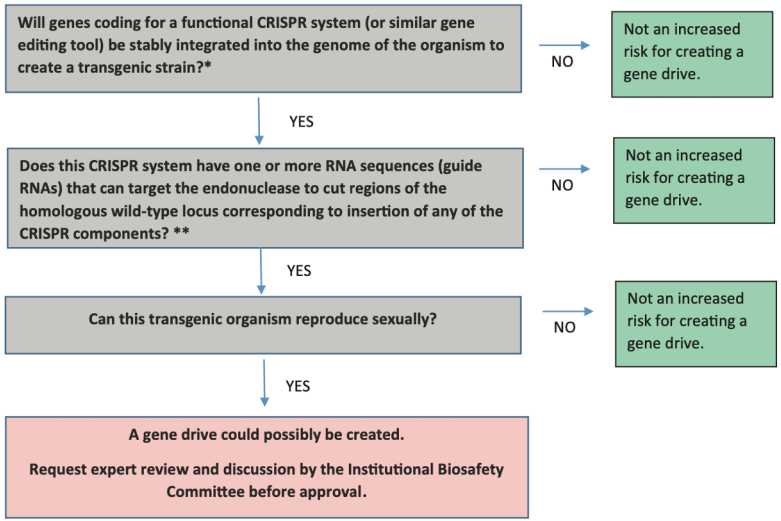


Figure 1. Is a gene drive being created? *The components of the functional CRISPR system—which include a catalytically active endonuclease (eg, Cas9 or similar), guide RNA sequences that bind to the endonuclease, and/or edited sequences of the target gene to replace—need not be present together. If these components are split, there is still a possibility of creating a gene drive due to recombination. **For a diagrammatic explanation of this question, refer to Figure 1 in Esvelt et al.[4]

Expertise level and quality of IBC review processes is not equal or standardized across institutions.

Challenges for BSOs and IBCs when reviewing research and determining appropriate containment and risk mitigation strategies without a full understanding of the risks.

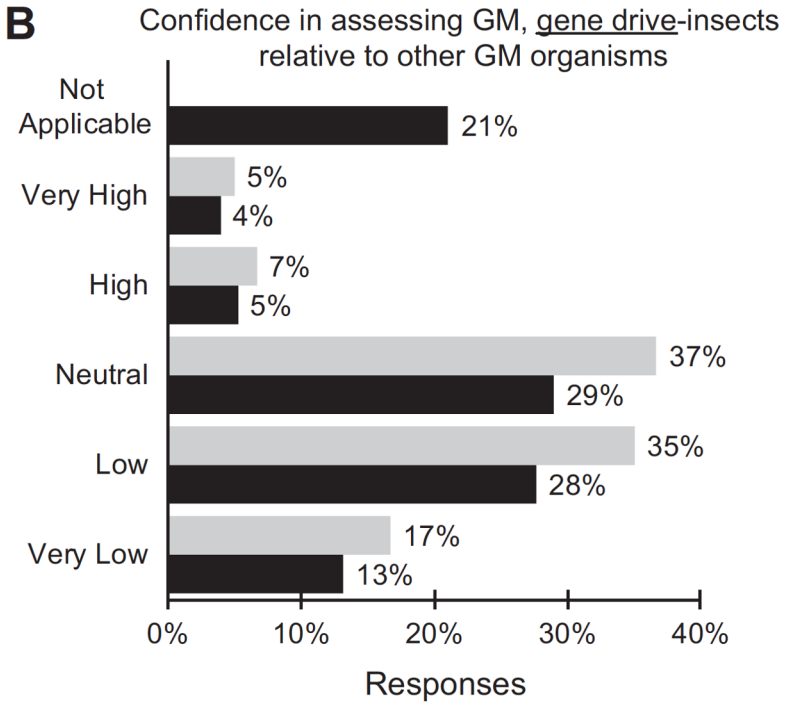
Krishnan, P. and D. Gillum. "Gene Drive 101: a basic guidance resource for biosafety professionals." *Applied Biosafety* 22.4 (2017): 181-184.

BSOs, IBCs and Understanding of Gene Drives

O'Brochta, D. A., et al. "A cross-sectional survey of biosafety professionals regarding genetically modified insects" *Applied Biosafety* 25.1 (2020): 19-27.

Authors identified challenges to conducting effective risks assessments of gene drives.

BSOs expressed a lack of confidence, primarily due to a lack of knowledge and experience, in their risk assessment for gene drive research.



ABSA International Gene Drives Education and Training Courses

Webinars

2017: Gene editing, CRISPR, and Gene Drives: Biosafety Considerations
2017: Synthetic Biology, Genome Editing Technologies, and Gene Drives
2018: Gene editing, CRISPR, and Gene Drives: Biosafety Considerations
2019: An Introduction to Synthetic Biology

Courses

2016: Synthetic Biology, Genome Editing Technologies, and Gene Drives (49 attendees)
2017: Gene Editing and Risk Assessment—Application to IBC Protocol Review (48 attendees)
2017: Human Gene Transfer—Biosafety Considerations (30 attendees)
2018: Gene Editing, Logic Gates, and SynBio in Human Gene Transfer (22 attendees)
2018: Gene Editing and Risk Assessment—Application to IBC Protocol Review (47 attendees)
2019: Gene Editing and Risk Assessment—Application to IBC Protocol Review (37 attendees)

Roles in assessing gene drive research

Principal Investigators bear the **primary responsibility** for understanding and **assessing the risks of their own work**, including with gene drives.

BSOs and IBCs work together to review the proposed research, assess the risks, and **determine the appropriate containment facilities and risk mitigation**.

BSOs and IBCs generally have **extensive experience in physical containment (i.e., barrier confinement)** principles and practices to safely conduct research with genetically modified organisms and pathogens.

Many PIs, BSOs and IBCs **do not fully understand the biological containment (i.e., molecular, ecological, reproductive confinement)** strategies for gene drive research.

There are challenges in conducting risk assessments for different gene drive experiments.

Is existing biosafety guidance adequate to address contained research with gene drives?

Physical containment (i.e., barrier confinement) guidance: Yes. BSOs and IBCs understand how to contain organisms. Containment practices, facilities and equipment are no different for gene drive research.

However, there is a **lack of guidance on how to thoroughly assess the risks** (e.g., which experiments pose a higher risk and thus warrant a higher level of containment?).

There is often insufficient data to support a robust risk assessment (e.g. effectiveness of molecular, ecological, or reproductive confinement strategies).

It would be extremely helpful to provide **standardized risk assessment tools** and **guiding principles** to assist PIs, BSOs and IBCs in assessing and managing risks.

Would additional physical containment guidance for certain species be useful?

There is good guidance in the Arthropod Containment Guidelines. However, they are **not mandatory** so institutions may or may not use them.

There may be value in incorporating the ACG into the NIH Guidelines.

There is a lack of guidance for species other than arthropods.

Provide guidance for the **most common species** used in gene drive experiments as well as those experiments in species that pose the **highest risk to society and the environment.**

Are existing general principles for biosafety risk assessment and management adequate?

No. There is a **lack of data** and uncertainty surrounding what a "**good risk assessment"** should look like for gene drives.

A general scientific consensus is needed to help PIs, BSOs and IBCs better determine—and thus manage—the risk associated with gene drives.

Tools for conducting risk assessments, training, and education opportunities **are needed.**

In addition, **communities of practitioners** and forums to **share knowledge** and experience **would be beneficial**.