Request for Public Comments on Proposed Amendments to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

August 9, 2023 – October 10, 2023

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Submit date: 8/15/2023

I am responding to this RFI: On behalf of myself

Name: Jackson Champer

Name of Organization: Peking University

Type of Organization: University

Role: Scientific researcher

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

I am a gene drive researcher. Different gene drives have vastly different ability to spread. Zero-threshold unconfined drives such as homing drives should get similar treatment the that described in these guidelines. However, there may be some conditions where less stringent confinement would be warranted. Here are some possibilities:

1. The species does not live in the area around the lab where an accidental escape could occur.

2. The gene drive somehow could not spread effectively in wild populations, such as by use of incompatible insect strains or a synthetic DNA as its target site.

3. The gene drive is designed to be intrinsically self-limiting, such as a split drive.

4. The gene drive is designed to be intrinsically confined with an introduction threshold, below which the drive cannot spread.

2. Comment - **NIH is seeking input on its proposals:**

Submit date: 8/24/2023

I am responding to this RFI: On behalf of an organization

Name: Brinda Dass

Name of Organization: Foundation for the national institutes of health- Gene Convene Global Collaborative

Type of Organization: Other

Type of Organization-Other: NGO

Role: Scientific researcher

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

Section I-E. General Definitions

Section I-E-7.

Currently states-

“Gene drive” is defined as a technology whereby a particular heritable element biases inheritance in its favor, resulting in the heritable element becoming more prevalent than predicted by Mendelian laws of inheritance in a population over successive generations.

This definition is misleading in that gene drive in itself is not a technology and gene drives exist in nature regardless of biotechnology using such elements to drive cargo for defined purposes. Engineered gene drive is when this phenomenon is harnessed using biotechnology to achieve the biased inheritance of chosen sequences. We would prefer the definition be amended to read as “Engineered Gene Drive” and by extension “Engineered Gene Drive Organisms”. This would also be aligned with international terminology currently in use such as the United Nations Convention on Biological Diversity and the Cartagena Protocol on Biosafety. Please also note the definitions in the scientific articles referenced below.

Standardizing the definition of gene drive Luke Alphey et al. https://doi.org/10.1073/pnas.2020417117

A gene drive is a gene drive: the debate over lumping or splitting definitions. Stephanie L James et al. Nature Communications 2023 https://doi.org/10.1038/s41467-023-37483-z

Gene Drive: Evolved and Synthetic. Austin Burt and Andrea Crisanti. ACS Chem. Biol. 2018, 13, 2, 343–346 https://doi.org/10.1021/acschembio.7b01031

Section II-A-3. Comprehensive Risk Assessment

States that-

Specific attention must be paid to risks of an unintended release from the laboratory and the potential impact on humans, other populations of organisms, and the environment.

Considerations for conducting risk assessments for research involving gene drive modified organisms might include:

d. Whether it is possible to predict the consequences of a construct, including the recognition of an unintended gene drive (i.e., construct not specifically designed as a gene drive but nonetheless having properties of a gene drive) and the possible consequences of escape into the environment;

e. The potential ability of the gene drive to spread or persist in local populations;

While there is definite value in conducting a risk assessment including potential ecosystem impacts

(with reference to Section V-N

Determination of whether a gene drive modified organism has a potential for serious detrimental impact on managed (agricultural, forest, grassland) or natural ecosystems)

as described above, there is concern as to the capacity of individual IBCs to take on such work on their own and the potential cost if consultants

(with reference to Section IV–B–2–a–(1).

When the institution conducts research involving gene drive modified organisms the institution must ensure that the Institutional Biosafety Committee has adequate expertise (e.g., specific species containment, ecological or environmental risk assessment) using ad hoc consultants if necessary.)

will be needed to provide the necessary depth of expertise and experience particularly where there is limited history of use and prior information. It would be helpful to point IBCs to existing guidance on ecological risk assessment conduct and reporting that would be considered acceptable.

2. Comment - **NIH is seeking input on its proposals:**

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/comments-to-FR-notice-on-NIH-Guidelines-changes-24-Aug-2023.docx

Submit date: 9/5/2023

I am responding to this RFI: On behalf of myself

Name: Anthony A. James

Name of Organization: University of California, Irvine

Type of Organization: University

Role: Scientific researcher

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

Please see attached PDF.

2. Comment - **NIH is seeking input on its proposals:**

Please see attached PDF.

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/AAJames-comments-to-proposed-changes-to-NIH-gene-drive-2023-17178.pdf

Description: Specific comments to sections of the proposed changes.

Submit date: 9/12/2023

I am responding to this RFI: On behalf of myself

Name: Rebeca Rodrigues dos Santos Silva

Name of Organization: Membros do Institutional Biosafety Committee (IBC) do HCFMUSP

Type of Organization: Not applicable

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

Como forma de contribuição, cito o plano de ação para experimentos e atividades utilizando a tecnologia do DNA recombinante, com uma proposta de "minimizar os riscos em atividades envolvendo a tecnologia do DNA recombinante", de forma adequada e alinhada com todos envolvidos no mesmo

meio, através dos seguintes passos.

Planejar: Analisar os procedimentos operacionais padrão e a partir deles planejar o experimento;

Fazer: Coloque as ações planejadas em execução;

Checar: Mensure os resultados das ações; Agir: Entenda e corrija o que não ocorreu como o planejado e padronize o que deu certo.

Para implementar essa medida, devemos manter todos envolvidos informados de forma clara e coerente.

Translation of comment as provided by Rebecca Rodrigues on 9/15/23:

As a form of contribution, I quote the action plan for experiments and activities using recombinant DNA technology, with a proposal to "minimize the risks in activities involving recombinant DNA technology", in an appropriate way and in harmony with everyone involved. Half, through the following steps. Plan: Analyze standard operating procedures and use them to plan the experiment; Do: Implement planned actions; Verify: Measure the results of actions; Act: Understand and correct what didn't happen as planned and standardize what worked. To implement this measure, we must keep everyone involved informed in a clear and coherent way.

2. Comment - NIH is seeking input on its proposals:

Submit date: 10/2/2023

I am responding to this RFI: On behalf of myself

Type of Organization: Nonprofit research organization

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

Does "gene drive animal" mean all transgenic animals? For example, would transgenic mice now need to be housed at BL-2N? Please clarify the language in III-D. As written, this is not feasible and the risk for transgenic mice being housed at BL-2N is very low.

2. Comment - **NIH is seeking input on its proposals:**

Submit date: 10/2/2023

I am responding to this RFI: On behalf of myself

Name: Major Eldridge

Type of Organization: Not applicable

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

I appreciate the new committee requirement. Having a gene drive expert on the committee is not only logical, but ensures the credibility of the Biosafety Committee.

2. Comment - **NIH is seeking input on its proposals:**

I think these are good additions. If changing the language is suggested by the scientific community majority, then I am for it. I am also a proponent for reclassifying WNV and SLEV.

Submit date: 10/5/2023

I am responding to this RFI: On behalf of myself

Name: Jeffrey D. Cirillo

Name of Organization: Texas A&M University

Type of Organization: University

Role: Scientific researcher

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

1) Minimum containment is already addressed in existing NIH guidelines, so no changes are needed. The only time additional scrutiny would potentially be needed is when release into the environment is expected. Otherwise, the additional administrative burden and cost is not warranted.

2) Risk assessment guidelines are already outlined well within NIH and BMBL guidelines, making additional guidelines duplicative, confusing and unwarranted.

3) Changes to the IBC and BSO are not needed. Educational opportunities may be necessary if they do not understand the technologies involved, but that could be addressed by standard notification procedures from NIH within their guidelines. Adding a clear description of the issue and technologies involved into the NIH guidelines would suffice.

2. Comment - **NIH is seeking input on its proposals:**

1. This change seems reasonable, since systems is more broad than viruses and clarifies that not only viruses can be used and would fit within this category.

2. This seems like a very reasonable re-classification to finalize, particularly since this level of containment has already been approved at several institutions as the result of risk assessment.

Submit date: 10/5/2023

I am responding to this RFI: On behalf of myself

Name: Stephen J Libbuy

Name of Organization: Stephen Libby PhD Consulting LLC

Type of Organization: Other

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

The changes and issues addressed in the proposal are all clear and appropriate.

2. Comment - **NIH is seeking input on its proposals:**

This clears up a lot of confusion for IBC members and reviewers.

The pointing to the BMBL6th edition for additional guidance is very appropriate. The NIH Guidelines do not address the specifics of laboratory safety.

Well Done!

Submit date: 10/6/2023

I am responding to this RFI: On behalf of an organization

Name: Andrea Ladd

Name of Organization: University of Wisconsin

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

2. Comment - **NIH is seeking input on its proposals:**

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/IBC-comment_Proposed-changes-to-the-NIH-Guidelines_100623.pdf

Description: Attached is a letter from the University of Wisconsin-Madison Institutional Biosafety Committee.

Submit date: 10/6/2023

I am responding to this RFI: On behalf of an organization

Name: Rachel Hodges

Name of Organization: BioPhorum

Type of Organization: Other

Type of Organization-Other: Biopharmaceutical Collaboration

Role: Scientific researcher

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

2. Comment - NIH is seeking input on its proposals:

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/BioPhorum-feedback-NIH-draft-proposals-to-research-involving-nucleic-acid-molecules.pdf

Submit date: 10/6/2023

I am responding to this RFI: On behalf of an organization

Name: Lesley Decker

Name of Organization: University of Washington

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

2. Comment - NIH is seeking input on its proposals:

Our feedback is in the attached PDF. Thank you.

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/Univ-Washington_Feedback-on-2023-proposed-NIH-Guidelines-changes.pdf

Description: Our feedback is in the attached PDF. Thank you.

Submit date: 10/6/2023

I am responding to this RFI: On behalf of an organization

Name: Kristin West

Name of Organization: COGR

Type of Organization: Other

Type of Organization-Other: non-profit association

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

Please see attached letter for comments.

2. Comment - **NIH is seeking input on its proposals:**

Please see attached letter for comments.

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/signed-response-to-NIH-Guidelines-re-synthetic-molecules.pdf

Description: Comments from COGR re. Proposed Amendments to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

Submit date: 10/7/2023

I am responding to this RFI: On behalf of myself

Name: Randy A. Albrecht

Name of Organization: Icahn School of Medicine at Mount Sinai

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

I thank the NIH for the opportunity to provide my personal comments on the proposed amendments to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines).

I am supportive of establishing BSL-2/ABSL-2 as the minimum containment requirement for research involving gene drive-modified organisms (GDMOs).

The proposed amendments should address Section IV-B-1-c of Section IV-B, Responsibilities of the Institution, of the NIH Guidelines. Section IV-B-1-c should be updated, correspondingly, to reflect the new requirement for a BSO in oversight of research involving GDMOs, which may be conducted at BSL-2/ABSL-2.

Section IV-B-3, Biological Safety Officer (BSO), of the NIH Guidelines should be amended to define the basic qualifications of the BSO consistent with the evolving landscape of life sciences research, such as research involving GDMOs, enhanced pathogens with pandemic potential, and gain-of-function research of concern (GoFRoC). Currently, The Laboratory Safety Monograph, A Supplement to the NIH Guidelines for Recombinant DNA Research, July 1978, set forth the basic qualifications of the BSO on page 192. The qualifications of the BSO should be updated and clearly described within the main body of the NIH Guidelines.

Section IV-B-3-b of Section IV-B, Biological Safety Officer (BSO), should be amended to require appointment of a BSO if it engages in recombinant or synthetic nucleic acid molecule research at BL2, BL3 or BL4. The landscape of life sciences research and translational biomedical research, specifically human gene therapy, that is conducted at BL2 is expanding. Gain-of-function or dual use research is not limited to research conducted at BL3 or BL4. The proposed changes to the NIH Guidelines stipulate that research on Gene Drive Modified Organisms (GDMOs) should be conducted at minimum at BL2. Requiring an institutional appointment of a BSO if it engages in recombinant or synthetic nucleic acid molecule research at BL2 would avoid potential gaps in oversight by the BSO and strengthen the role of the BSO in oversight of life sciences research.

The application of the NIH Guidelines should extend beyond life sciences research funded by the NIH. For example, the National Science Foundation endorses the NIH Guidelines and requires funding applicants to adhere to the NIH Guidelines. There are ongoing public policy discussions regarding the limitation of federal oversight of gain-of-function and dual use life sciences that is not funded by the U.S. Government. Extending the application of the NIH Guidelines to all research funded by the U.S.

Government would be consistent at least with federal oversight of gain-of-function and dual use life sciences research.

Currently, the PHS398 forms for NIH grant/contract applications document institutional oversight of Human Subjects Research and Vertebrate Animals by documenting approval dates and assurance numbers of the IRB and IACUC, respectively. However, there are no equivalent questions regarding institutional oversight by the IBC of proposed research that may involve use of recombinant DNA or synthetic nucleic acids, and the equivalent registration of the IBC with the NIH OSP. The potential gap in this oversight pertains to the likelihood that a NIH application contains preliminary data generated from life sciences research that likely required IBC approval. The current NIH practice is to require that the applicant include a biohazard/biosafety statement somewhere in the application and then inquire about the IBC approval status during the just-in-time notice of NIH award of funding. These practices are not consistent with the NIH Guidelines, do not ensure the IBC has reviewed and approved the research, and has potential to undermine the oversight authority of the IBC. Amending the NIH grant/contract application forms to capture IBC approval status at the time of application submission would strengthen institutional oversight of biomedical research. Furthermore, this amendment would be consistent with the potential changes to the Policies for Oversight of Dual Use Research of Concern (DURC) and the Potential Pandemic Pathogen Care and Oversight (P3CO) policy framework and proposed bottom-up approach to institutional oversight of gain-of-function research of concern (GoFRoC), Federal Register Document Number 2023-18906.

2. Comment - **NIH is seeking input on its proposals:**

Submit date: 10/9/2023

I am responding to this RFI: On behalf of an organization

Name: Rebecca Moritz

Name of Organization: American Biological Safety Association International

Type of Organization: Professional org association

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

2. Comment - NIH is seeking input on its proposals:

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/ABSA-Comments-GDMO-10.9.23.pdf

Submit date: 10/9/2023

I am responding to this RFI: On behalf of myself

Name: Zach Adelman

Name of Organization: Texas A&M University

Type of Organization: University

Role: Scientific researcher

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

I support all of the indicated changes.

2. Comment - NIH is seeking input on its proposals:

I agree with the change in classification from "Helper viruses" to helper systems, as well as the reclassification of WNV and SLEV to RG2.

However, there seems to be a legacy mistake that has glided through the various editions of the NIH Guidelines for at least the past 40 years and should finally be corrected.

SLEV is listed under the Alphaviruses (Togaviruses). However, SLEV is not a member of this virus family. SLEV, like WNV, is a member of the family Flaviviridae, genus Flavivirus (now considered genus Orthoflavivirus).

https://ictv.global/report/chapter/flaviviridae/flaviviridae

Submit date: 10/9/2023

I am responding to this RFI: On behalf of an organization

Name: Sheryl Mansour

Name of Organization: University of California, San Diego

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

The proposed addition of Gene Drive Modified Organisms (GDMO) into the NIH Guidelines provides guidance and instruction on institutional oversight and biosafety for research with an emergency technology that has a complex risk profile. Updates include specific requirements or expectations placed on the researcher, biosafety officer, IBC, and institution. Some of these expectations add complexity to the oversight mechanism, reduce the IBC's ability to conduct risk assessment based biosafety level determinations, and create more questions on how to appropriately implement the NIH Guidelines.

IBC's are aware of limitations to finding subject matter expertise in the field of gene drive. Additional clarity and guidance on selection of Ad Hoc reviewers will support institutions to supplement expertise when necessary. It is highly encouraged that the NIH OSP consider equity and access to Ad Hoc subject matter expertise for institutions of all sizes and research profiles.

2. Comment - **NIH is seeking input on its proposals:**

Can a definition of helper system be added into definitions Section of the NIH Guidelines? The Federal Register justification provided examples like "helper systems (e.g., transient transfection systems, packaging cell lines, replicon systems, etc.)". This will aid institutions in ensuring the helper system is evaluated appropriately under this section of the NIH Guidelines.

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/Complete_with_DocuSign_UCSD_Comments_for_NIH.pdf

Description: UCSD IBC Comments for NIH Office of Science Policy

Submit date: 10/9/2023

I am responding to this RFI: On behalf of myself

Name: Philip Barruel

Name of Organization: UC Davis

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

Section I-E-7 – The definition of "gene drive" states, "a particular heritable element biases inheritance in its favor..." implies that the organisms have alleles for certain genes involved. Does the definition of "gene drive" exclude prokaryotes?

Section II-A-3 – The text, "The appropriate containment level may be equivalent to the Risk Group classification of the agent, or it may be raised or lowered as a result of the above considerations" seems to contradict the latter statement about minimum containment level as BL2. I acknowledge that this text is not new but the proposed changes to this section is in this context. It can be confusing if GDMO is read in this context.

Section II-A-3-3 – The reference to "more stringent containment measures" is vague. Do local IBCs have leeway to determine what "more stringent" means, or is there an acceptable definition for that term?

Section III-D-4 –Requires the minimum requirement of BL2 for gene drive modified animals. I realize this is referring to the NIH Guidelines “BL2-N” and not the BMBL ABSL-2. But from the perspective of BMBL (6th ed.) the key differences between ABSL-1 and ABSL-2 are biosafety cabinet and an autoclave in the ABSL-2 facility. Gene drive modified animal containment is not why a biosafety cabinet is recommended for ABSL-2, it is for when animals infected with Risk Group 2 microorganisms. Presence of an autoclave in the facility is not what is key to containment, it is having barriers that help keep escaped animals from escaping and appropriate inactivation of the gene drive modified animal (e.g., incineration of rodent carcasses).

Section III-D and III-E – A colleague mentioned that there are some gene drives that are used where the drive is silenced or spliced out in future offspring (whether animals or plants), please comment to verify that this “feature” takes these organisms outside of the definition of GDMO.

Section IV-B-1-c – This adds an IBC member for the GDMO area of expertise. Can this new IBC member be an ad hoc member who can be activated only when there’s a GDMO IBC protocol under review? Also, can we use experts from a partner institution (regardless of distance from our institution)? It is possible that the IBC protocol submission is from the expert within our institution and this can create a conflict of interest. Having the ability to ask an expert in a partner institution provides a to address the conflict of interest.

2. Comment - **NIH is seeking input on its proposals:**

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Sepideh Sefidvash-Hockley

Name of Organization: Penn State University

Type of Organization: University

Type of Organization-Other:

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

- Imperative all material must be submitted to the IBC regardless of the BSL level. (BSL 1, BSL 2, BSL 2+, BSL 3, BSL4). A campaign by all participating universities to ensure all faculty , post docs, etc. are aware of the need for a thorough review

o Explicit SOP would also be required so a proper risk assessment can be completed by the scientific members of the committee, IBC Chair and Institutional Biosafety Officer

- Significant items to consider will be ;
- the working experience of staff manipulating the material
- Specific facility capabilities

o Self-closing door

o Sink with eyewash

- Properly certified BSC
- Properly maintained laboratory equipment.
- Initial Lab Survey/Inspection. Repeat annually or possible semi annually depending on the risk after the assessment

o Complete understanding of decontamination and waste disposal process, as well as the spill and exposure response by the PI, the individual and the entire lab staff.

o Each institution should also consider adding a specific section on their approval protocol specifically designed to focus in on the gene drive technology.

Section I-E-7 Clarity is needed on the definition of gene drives and gene drive technology IBCs and PIs have a better understanding of their roles and responsibilities. As written, the definition does not clearly define a gene drive's capabilities.

2. Comment - **NIH is seeking input on its proposals:**

- The changes regarding the helper system wording addition over helper virus seems like a good idea. The helper systems may stimulate the PI to provide all information regarding their project.

- The WNV and SLEV risk group upgrade also seems good so it is submitted appropriately by the PI. In these cases you would want to be "extra" sure you know the cradle to grave pathway of the material, especially if they are used in animals for expression. (transport, housing, waste handling, decontamination, waste disposal, spill and clean up, decontaminating equipment.

The risk assessment information within section 11_A-3, are defined enough so an acceptable assessments can be done.

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Malissa Mayer-Diaz, MS, MSPH

Name of Organization: University of Texas Medical Branch

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

For Part 1), regarding proposed changes to Section III-D-4, we welcome the clarification in the first paragraph that makes it obvious that "deliberate transfer of recombinant or synthetic nucleic acid molecules …into whole animals" is covered in this Section.

For Part 1), regarding the proposed changes to Section III-E-3, we object strongly to the addition of the words "or use" to this Section, to read "This section covers experiments involving the generation or use of rodents …" (emphasis added). There is no justification provided from the agency for the broadening of experiments covered by this Section. There is no risk assessment provided from the agency on why the use of transgenic rodents should be covered by the NIH Guidelines. The request for information does not even discuss this change to Section III-E-3, stating only "Section III-E-3 is proposed to be amended to reference the new Section III-D-8 to reinforce that research with GDMOs shall be conducted at a minimum of BL2." We understand that there are risks to personnel, the animal, the community, and the environment when generating transgenic rodents. We do not understand why the agency is proposing to expand Section III-E-3 to include the use of transgenic rodents.

2. Comment - **NIH is seeking input on its proposals:**

We are ambivalent on the change from "helper viruses" to "helper systems". If this proposed change is enacted, we would appreciate if the agency would either provide a definition for helper systems or keep the examples provided in the RFI: "However, helper systems (e.g., transient transfection systems, packaging cell lines, replicon systems, etc.) are more commonly used than a helper virus" (emphasis added).

We welcome the harmonization of the risk group for WNV and SLEV in the NIH Guidelines to the containment guidance provided in the BMBL. We expect that this will reflect the required safe handling of these agents. We expect this will reduce administrative burden for our investigators who would like to work with recombinant versions of these agents and currently require NIH approval to work with them at BSL2.

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Leah Buchman

Name of Organization: Biotechnology Innovation Organization

Type of Organization: Professional org association

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

2. Comment - NIH is seeking input on its proposals:

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/BIO-Comments_NIH-Proposed-GDMO-Research-Guidelines_-Final.pdf

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: LBNL Institutional Biosafety Committee

Name of Organization: Lawrence Berkeley National Lab

Type of Organization: Other

Type of Organization-Other: Federally funded research and development center

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

Please see attached file

2. Comment - **NIH is seeking input on its proposals:**

Please see attached file

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/Lawrence-Berkeley-National-Lab-Comments-for-NIH-Proposed-Updates.docx

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Thomas Leach

Name of Organization: New Jersey Association for Biomedical Research

Type of Organization: Professional org association

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

On behalf of the members of the New Jersey Association for Biomedical Research (NJABR), whose members include the nation's leading life sciences companies and research universities, thank you for the opportunity to comment on the proposal to revise the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) to include specific considerations and requirements for conducting research involving gene drive modified organisms (GDMO) in contained research settings.

NJABR has a concern regarding the proposed changes to the NIH Guidelines in Section III-E-3 3 (Experiments Involving Transgenic Rodents). Specifically, the words "or use" are included in the first sentence in this subsection and is proposed to read as follows: "This section covers experiments involving the generation or use of rodents in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic rodents)." In particular, NJABR is concerned that the inclusion of the words "or use" in the NIH Guidelines will add significant, unnecessary administrative and practical burdens to researchers and institutional administrative and compliance staff. This contradicts directives in the 21st Century Cures Act, and we urge NIH to reconsider the need for the inclusion of the words "or use" in this section.

NJABR recognizes that the addition of "or use" in Section III-E-3 3 can also be utilized to qualify that Section III-E-3 3 is intended to cover the generation and subsequent use of an in-house generated transgenic rodents. If this is NIH's intent, we respectfully ask that additional language be added to make this more clear to ensure the language is not unnecessarily interpreted.

Thank you for reviewing our brief comments on this matter. If you have any questions, please do not hesitate to contact me.

Sincerely,

Thomas A. Leach

Executive Director

2. Comment - **NIH is seeking input on its proposals:**

Submit date: 10/10/2023

I am responding to this RFI: On behalf of myself

Name: Adrienne E. Zweifel

Name of Organization: University of California

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

The proposed addition of Gene Drive Modified Organisms (GDMO) into the NIH Guidelines provides guidance and instruction on institutional oversight and biosafety for research with an emergency technology that has a complex risk profile. Updates include specific requirements or expectations placed on the researcher, biosafety officer, IBC, and institution. Some of these expectations add complexity to the oversight mechanism, reduce the IBC's ability to conduct risk assessment based biosafety level determinations, and create more questions on how to appropriately implement the NIH Guidelines.

- NIH Guidelines, Section I-E-7 – The definition of "gene drive" states, "a particular heritable element biases inheritance in its favor..." implies that the organisms have alleles for certain genes involved. Does the definition of "gene drive" exclude prokaryotes?

- NIH Guidelines, Section II-A-3:

The text, "The appropriate containment level may be equivalent to the Risk Group classification of the agent, or it may be raised or lowered as a result of the above considerations" seems to contradict the latter statement about minimum containment level as BL2. I acknowledge that this text is not new but the proposed changes to this section is in this context. It can be confusing if GDMO is read in this context.

In the risk assessment section of the proposed updates, what is considered biosafety data? Is it publications showing attenuated gene drives or safety data on the specific selected gene drive? Publications may not be available and institutions may want pilot projects to be performed by the researcher to provide biosafety data. Recommend inclusion of guidance for pilot projects that would provide biosafety data.

- NIH Guidelines, Section II-A-3-3 – The reference to "more stringent containment measures" is vague. Do local IBCs have leeway to determine what "more stringent" means, or is there an acceptable definition for that term?

- NIH Guidelines, Sections IIID and IIIE – There are some gene drives that are used where the drive is silenced or spliced out in future offspring (whether animals or plants), please comment to verify that this "feature" takes these organisms outside of the definition of GDMO.

- NIH Guidelines, Section III-D-8:

Some organisms and life stages of organisms would have greatly reduced risk of accidental release into the environment. Setting a minimum BSL reduces an institution's ability to perform a risk assessment

based on the research, facility containment, etc. and determine an appropriate biosafety level. The broad range of possible targets for the creation of GDMO do not all warrant immediate assignment at BSL-2/N/P/AC.

Gene drive technology is advancing toward a more managed and control approach, improving safety and reducing risk to the environment. There are gene drives used to create GDMO where the drive is silences or spliced out in future offspring or requires an unnatural mechanism to engage the gene of interest. It should be up to the Principle Investigator and Institutional Biosafety Committee to perform a risk assessment and determine when an organism is considered a Gene Drive Modified Organism and when the offspring would no longer meet the definition of GDMO. Clarification from the NIH on what is a GDMO is necessary as gene drive technology advances.

Will there be a process for downgrade requests to the NIH Office of Science Policy? A request for downgrade is described under Section III-D-4. Recommend adding this option to Section III-D-8.

- NIH Guidelines III-E-3:

Would this require that all offspring from GDMO be handled at ABSL-2? There are gene drives used to create transgenic mice where the drive is silences or spliced out in future offspring. It should be up to the Principle Investigator and Institutional Biosafety Committee to perform a risk assessment and determine when an organism is considered a Gene Drive Modified Organism. Clarification from the NIH on what is a GDMO is necessary.

Recommend updating the FAQs for Research on Genetically Modified (Transgenic) Animals.

- NIH Guidelines, Section IV-B-2-a-(1):

There are limited "Gene Drive" experts in the field and often at smaller institutions the lone expert is the single PI submitting a gene drive BUA. Can the NIH provide clarity on Ad Hoc reviewers for an IBC? Does an Ad Hoc reviewer need to be local? What are the anticipated qualifications to be an Ad Hoc Reviewer?

- NIH Guidelines, Section V-N:

Can the NIH provide clarity on Ad Hoc reviewers for an IBC? Many institutions will need to use an Ad Hoc. Does an Ad Hoc reviewer need to be local? What are the anticipated qualifications to be an Ad Hoc Reviewer?

When describing managed or natural ecosystems, this wording would be better addressed by discussing impact to local environment and ecosystems in cases of accidental release.

- NIH Guidelines Section III, F-8 Appendix C-III-A:

This section will now require NIH exempt work with Saccharomyces and gene drive to be covered under III-D and reviewed and approved by the IBC prior to start of work. This is an undue burden for an agent that was previously exempt at BSL-1 to now require IBC approval prior to start of work at BSL-2. Would the NIH consider the agents listed under III-F-8 Appendix C as possibly being under III-E and BSL-1 when used as a gene drive modified organism?

- NIH Guidelines Section III-F-8 Appendix C-IV-A:

This section will now require NIH exempt work with Saccharomyces and gene drive to be covered under III-D and reviewed and approved by the IBC prior to start of work. This is an undue burden for an agent that was previously exempt at BSL-1 to now require IBC approval prior to start of work at BSL-2. Would the NIH consider the agents listed under III-F-8 Appendix C as possibly being under III-E and BSL-1 when used as a gene drive modified organism?

If implemented, the proposed updates to the NIH Guidelines would impede vital research efforts. Given the stringent biosafety regulations and thorough risk assessment by the IBCs, requiring a specific Biosafety Level for containment of GDMO, without a process for lowering the BSL based on risk, limits the ability of the IBC to operate as designed, and would also raise research costs and impede the cost-effectiveness of NIH-sponsored research.

IBC's are aware of limitations to subject matter expertise in the field of gene drive. Additional clarity and guidance on selection of Ad Hoc reviewers will support institutions to supplement expertise when necessary. It is highly encouraged that the NIH OSP consider equity and access to Ad Hoc subject matter expertise for institutions of all sizes and research profiles.

2. Comment - **NIH is seeking input on its proposals:**

- NIH Guidelines, Section: III-D-3 and III-E-1

Can a definition of helper system be added into definitions Section of the NIH Guidelines? The Federal Register justification provided examples like "helper systems (e.g., transient transfection systems, packaging cell lines, replicon systems, etc.)". This will aid institutions in ensuring the helper system is evaluated appropriately under this section of the NIH Guidelines.

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Thomas Leach

Name of Organization: Pennsylvania Society for Biomedical Research

Type of Organization: Professional org association

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

On behalf of the members of the Pennsylvania Society for Biomedical Research (PSBR), whose members include the nation's leading life sciences companies and research universities, thank you for the opportunity to comment on the proposal to revise the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) to include specific considerations and requirements for conducting research involving gene drive modified organisms (GDMO) in contained research settings.

PSBR has a concern regarding the proposed changes to the NIH Guidelines in Section III-E-3 3 (Experiments Involving Transgenic Rodents). Specifically, the words "or use" are included in the first sentence in this subsection and is proposed to read as follows: "This section covers experiments involving the generation or use of rodents in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic rodents)." In particular, PSBR is concerned that the inclusion of the words "or use" in the NIH Guidelines will add significant, unnecessary administrative and practical burdens to researchers and institutional administrative and compliance staff. This contradicts directives in the 21st Century Cures Act, and we urge NIH to reconsider the need for the inclusion of the words "or use" in this section.

PSBR recognizes that the addition of "or use" in Section III-E-3 3 can also be utilized to qualify that Section III-E-3 3 is intended to cover the generation and subsequent use of an in-house generated transgenic rodents. If this is NIH's intent, we respectfully ask that additional language be added to make this more clear to ensure the language is not unnecessarily interpreted.

Thank you for reviewing our brief comments on this matter. If you have any questions, please do not hesitate to contact me.

Sincerely,

Thomas A. Leach

Executive Director

2. Comment - **NIH is seeking input on its proposals:**

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Vanessa Cook

Name of Organization: UC Merced

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

The proposed addition of Gene Drive Modified Organisms (GDMO) into the NIH Guidelines provides guidance and instruction on institutional oversight and biosafety for research with an emergency technology that has a complex risk profile. Updates include specific requirements or expectations placed on the researcher, biosafety officer, IBC, and institution. Some of these expectations add complexity to the oversight mechanism, reduce the IBC's ability to conduct risk assessment based biosafety level determinations, and create more questions on how to appropriately implement the NIH Guidelines.

The IBC has compiled comments, questions, and concerns on updates to specific sections:

NIH Guidelines Section I-E:

Recommend adding the definition for a Gene Drive Modified Organism in Section I-E of the NIH Guidelines

NIH Guidelines Section II-A-3:

In the risk assessment section of the proposed updates, what is considered biosafety data? Is it publications showing attenuated gene drives or safety data on the specific selected gene drive? Publications may not be available and institutions may want pilot projects to be performed by the researcher to provide biosafety data. Recommend inclusion of guidance for pilot projects that would provide biosafety data.

NIH Guidelines Section III-D-8:

Some organisms and life stages of organisms would have greatly reduced risk of accidental release into the environment (e.g., zebrafish). Setting a minimum BSL for all gene drive organisms reduces an institutions ability to perform a risk assessment based on the research, facility containment, etc. and determine an appropriate biosafety level. The broad range of possible targets for the creation of GDMO do not all warrant immediate assignment at BSL-2/N/P/AC.

Gene drive technology is advancing toward a more managed and controlled approach, improving safety and reducing risk to the environment. There are gene drives used to create GDMO where the drive is silenced or spliced out in future offspring or requires an unnatural mechanism to engage the gene of interest. It should be up to the Principle Investigator and Institutional Biosafety Committee to perform a risk assessment and determine when an organism is considered a Gene Drive Modified Organism and when the offspring would no longer meet the definition of GDMO. Clarification from the NIH on what is a GDMO is necessary as gene drive technology advances.

Will there be a process for downgrade requests to the NIH Office of Science Policy? A request for downgrade is described under Section III-D-4. Recommend adding this option to Section III-D-8.

NIH Guidelines III-E-3:

Would this require that all offspring from GDMO be handled at ABSL-2? There are gene drives used to create transgenic mice where the drive is silences or spliced out in future offspring. It should be up to the Principle Investigator and Institutional Biosafety Committee to perform a risk assessment and determine when an organism is considered a Gene Drive Modified Organism. Clarification from the NIH on what is a GDMO is necessary.

Recommend updating the FAQs for Research on Genetically Modified (Transgenic) Animals.

NIH Guidelines IV-B-2-a-(1):

There are limited "Gene Drive" experts in the field and often at smaller institutions the only expert is the PI submitting a gene drive Biohazard Use Authorization (BUA). Can the NIH provide clarity on Ad Hoc reviewers of protocols involving gene drive for an IBC? Does an Ad Hoc reviewer need to be local? What are the anticipated qualifications to be an Ad Hoc reviewer? Do Ad Hoc reviewers serve solely as subject matter experts or are they voting members on gene drive protocols?

NIH Guidelines Section V-N:

Can the NIH provide clarity on Ad Hoc reviewers for an IBC? Many institutions will need to use an Ad Hoc. Does an Ad Hoc reviewer need to be local? What are the anticipated qualifications to be an Ad Hoc Reviewer? Do Ad Hoc reviewers serve solely as subject matter experts or are they voting members on gene drive protocols?

When describing managed or natural ecosystems, this wording would be better addressed by discussing impact to local environment and ecosystems in cases of accidental release.

NIH Guidelines Section III-F-8 Appendix C-III-A:

This section would now require NIH exempt work with gene drive in Saccharomyces cerevisiae to be covered under III-D and reviewed and approved by the IBC prior to start of work. This is an undue burden for an agent that was previously exempt and appropriate to be handled at BSL-1 to now require IBC approval prior to start of work at BSL-2 containment. Would the NIH consider the agents listed under III-F-8 Appendix C as possibly being under III-E and handled at BSL-1 when used as a gene drive modified organism?

NIH Guidelines Section III-F-8 Appendix C-IV-A:

This section would now require NIH exempt work with gene drive in Saccharomyces cerevisiae to be covered under III-D and reviewed and approved by the IBC prior to start of work. This is an undue burden for an agent that was previously exempt and appropriate to be handled at BSL-1 to now require IBC approval prior to start of work at BSL-2 containment. Would the NIH consider the agents listed under III-F-8 Appendix C as possibly being under III-E and handled at BSL-1 when used as a gene drive modified organism?

If implemented, the proposed updates to the NIH Guidelines would impede vital research efforts. Given the stringent biosafety regulations and thorough risk assessment by the individual university IBCs, requiring a specific Biosafety Level for containment of GDMO, without a process for lowering the BSL based on risk, limits the ability of the IBC to operate as designed, and would also raise research costs and impede the cost-effectiveness of NIH-sponsored research.

IBCs are aware of limitations to subject matter expertise in the field of gene drive. Additional clarity and guidance on selection of Ad Hoc reviewers will support institutions to supplement expertise when necessary. It is highly encouraged that the NIH OSP consider equity and access to Ad Hoc subject matter expertise for institutions of all sizes and research profiles.

2. Comment - NIH is seeking input on its proposals:

Request addition of definition of "helper system" into the definitions section of the NIH Guidelines. The Federal Register justification provided examples like â€œhelper systems (e.g., transient transfection systems, packaging cell lines, replicon systems, etc.)â€. This will aid institutions in ensuring the helper system is evaluated appropriately under this section of the NIH Guidelines.

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: James Baugh

Name of Organization: University of California Berkeley

Type of Organization: University

Role: Member of the public

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

The proposed addition of Gene Drive Modified Organisms (GDMO) into the NIH Guidelines provides guidance and instruction on institutional oversight and biosafety for research with an emergency technology that has a complex risk profile. Updates include specific requirements or expectations placed on the researcher, biosafety officer, IBC, and institution. Some of these expectations add complexity to the oversight mechanism, reduce the IBC's ability to conduct risk assessment based biosafety level determinations, and create more questions on how to appropriately implement the NIH Guidelines.

The IBC has compiled comments, questions, and concerns on updates to specific sections:

- NIH Guidelines Section I-E:

Recommend adding the definition for a Gene Drive Modified Organism in Section I-E of the NIH Guidelines

- NIH Guidelines Section II-A-3:

In the risk assessment section of the proposed updates, what is considered biosafety data? Is it publications showing attenuated gene drives or safety data on the specific selected gene drive? Publications may not be available and institutions may want pilot projects to be performed by the researcher to provide biosafety data. Recommend inclusion of guidance for pilot projects that would provide biosafety data.

- NIH Guidelines Section III-D-8:

Some organisms and life stages of organisms would have greatly reduced risk of accidental release into the environment. Setting a minimum BSL reduces an institutions ability to perform a risk assessment based on the research, facility containment, etc. and determine an appropriate biosafety level. The broad range of possible targets for the creation of GDMO do not all warrant immediate assignment at BSL-2/N/P/AC.

Gene drive technology is advancing toward a more managed and control approach, improving safety and reducing risk to the environment. There are gene drives used to create GDMO where the drive is silences or spliced out in future offspring or requires an unnatural mechanism to engage the gene of interest. It should be up to the Principle Investigator and Institutional Biosafety Committee to perform a risk assessment and determine when an organism is considered a Gene Drive Modified Organism and when the offspring would no longer meet the definition of GDMO. Clarification from the NIH on what is a GDMO is necessary as gene drive technology advances.

Will there be a process for downgrade requests to the NIH Office of Science Policy? A request for downgrade is described under Section III-D-4. Recommend adding this option to Section III-D-8.

- NIH Guidelines III-E-3:

Would this require that all offspring from GDMO be handled at ABSL-2? There are gene drives used to create transgenic mice where the drive is silences or spliced out in future offspring. It should be up to the Principle Investigator and Institutional Biosafety Committee to perform a risk assessment and determine when an organism is considered a Gene Drive Modified Organism. Clarification from the NIH on what is a GDMO is necessary.

Recommend updating the FAQs for Research on Genetically Modified (Transgenic) Animals.

- NIH Guidelines IV-B-2-a-(1):

There are limited "Gene Drive" experts in the field and often at smaller institutions the 1 expert is the 1 PI submitting a gene drive BUA. Can the NIH provide clarity on Ad Hoc reviewers for an IBC? Does an Ad Hoc reviewer need to be local? What are the anticipated qualifications to be an Ad Hoc Reviewer?

- NIH Guidelines Section V-N:

Can the NIH provide clarity on Ad Hoc reviewers for an IBC? Many institutions will need to use an Ad Hoc. Does an Ad Hoc reviewer need to be local? What are the anticipated qualifications to be an Ad Hoc Reviewer?

When describing managed or natural ecosystems, this wording would be better addressed by discussing impact to local environment and ecosystems in cases of accidental release.

- NIH Guidelines Section III-F-8 Appendix C-III-A:

This section will now require NIH exempt work with Saccharomyces and gene drive to be covered under III-D and reviewed and approved by the IBC prior to start of work. This is an undue burden for an agent that was previously exempt at BSL-1 to now require IBC approval prior to start of work at BSL-2. Would the NIH consider the agents listed under III-F-8 Appendix C as possibly being under III-E and BSL-1 when used as a gene drive modified organism?

- NIH Guidelines Section III-F-8 Appendix C-IV-A:

This section will now require NIH exempt work with Saccharomyces and gene drive to be covered under III-D and reviewed and approved by the IBC prior to start of work. This is an undue burden for an agent that was previously exempt at BSL-1 to now require IBC approval prior to start of work at BSL-2. Would the NIH consider the agents listed under III-F-8 Appendix C as possibly being under III-E and BSL-1 when used as a gene drive modified organism?

If implemented, the proposed updates to the NIH Guidelines would impede vital research efforts. Given the stringent biosafety regulations and thorough risk assessment by the IBCs, requiring a specific Biosafety Level for containment of GDMO, without a process for lowering the BSL based on risk, limits the ability of the IBC to operate as designed, and would also raise research costs and impede the cost-effectiveness of NIH-sponsored research.

IBC's are aware of limitations to subject matter expertise in the field of gene drive. Additional clarity and guidance on selection of Ad Hoc reviewers will support institutions to supplement expertise when necessary. It is highly encouraged that the NIH OSP consider equity and access to Ad Hoc subject matter expertise for institutions of all sizes and research profiles.

2. Comment - **NIH is seeking input on its proposals:**

- NIH Guidelines Section: III-D-3 and III-E-1

Can a definition of helper system be added into definitions Section of the NIH Guidelines? The Federal Register justification provided examples like "helper systems (e.g., transient transfection systems, packaging cell lines, replicon systems, etc.)". This will aid institutions in ensuring the helper system is evaluated appropriately under this section of the NIH Guidelines.

Uploaded File: https://osp.od.nih.gov/wp-content/uploads/ninja-forms/9/UCB-Comments-for-NIH-Proposed-Updates.docx

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Eve Granatosky

Name of Organization: American Society of Plant Biologists (ASPB)

Type of Organization: Professional org association

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

The American Society of Plant Biologists (ASPB), founded in 1924 as the American Society of Plant Physiologists, was established to promote the growth and development of plant biology, to encourage and publish research in plant biology, and to promote the interests and professional advancement of plant scientists in general. ASPB members conduct research to enhance understanding of plant biology and, among other applications, its impacts on public health and wellbeing. We welcome the opportunity to provide perspective from the plant biology research community on this important policy topic that impacts a range of biologists from many disciplines.

(3) ASPB is concerned with the proposed requirement for a Biosafety Officer (BSO) given any research involving gene drives. This requirement is in the amendment to Section IV-B-1-c and Section IV-B-3c. The original IV-B-1-c only requires a BSO if there is work at BSL3 or BSL4, or if it is performed on a large scale, and ASPB finds this requirement reasonable. However, considering NIH proposes that the minimum requirement for gene drive research would warrant BSL2, this additional requirement of a BSO would be unnecessarily onerous for research already conducted under BSL2 conditions.

ASPB agrees with NIH's proposal outlined in Section IV-B-2-a-(1) to require an institution conducting gene drive research have an Institutional Biosafety Committee with adequate expertise, but NIH's current language includes only human subject research. ASPB suggests this section be amended to delete mention of specific types of research and instead propose, for example, that "the institution must ensure that the Institutional Biosafety Committee has adequate expertise to assess the research projects for which it is responsible, using ad hoc consultants if necessary."

Thank you for the opportunity to comment, and please let us know if ASPB can provide additional assistance on this topic.

2. Comment - NIH is seeking input on its proposals:

n/a

Submit date: 10/10/2023

I am responding to this RFI: On behalf of an organization

Name: Ryan Lisk

Name of Organization: The University of Texas Southwestern Medical Center

Type of Organization: University

Role: Institutional official

1. Comment specific to the part of the proposal dealing with gene drive modified organisms:

We request clarification on whether the proposed minimum containment for Gene Drive Modified Organisms (GDMOs) at biosafety level 2 (BSL-2) is expected to be enforced retroactively. This may include reevaluation and/or reclassification of current work practices already in place with potential procedural changes for researchers. With respect to administrative impacts, the reclassification would likely place a strain on current Institutional Biosafety Committee (IBC) processes leading to extended review times and approvals. The potential fiscal implications remain unclear but may include hiring of additional staff to review research projects that qualify for the revised scope.

The proposed minimum containment for GDMOs at animal biosafety level 2 (ABSL-2) potentially has both fiscal and administrative impacts. Current processes place certain types of gene drive work (such as CRISPR) under biosafety level 1 (BSL-1) housing, to include work in both whole animals and arthropods. Movement of this work to BSL-2 containment for housing areas may require facility modification such as directional airflow, one-pass air, and potential retrofits of certain spaces to include biosafety cabinets (BSCs). Additionally, renovation of these spaces will increase expenditures that are currently not budgeted for. Administratively, the proposed changes have an impact on the scope of current institutional policies and SOPs and will require a significant amount of time to make implement those changes accordingly.

2. Comment - **NIH is seeking input on its proposals:**