Submission # 1:

Date	6/21/2021
Name	Dr. Anthony A. James
Organization:	University of California
Email:	aajames@uci.edu
Comment:	Pursuant to the Federal Register 'A Notice by the National Institutes of Health on 05/26/2021' the following comments are submitted in response to the above-referenced document. 1) I applaud the efforts of the working group to produce a draft that is generally well- considered and written. 2) **'Item 4.2 If NIH funds proposals that have, as part of the research strategy, a plan to conduct eventual field release, such proposals should articulate what the impact of the research will be even if field release ultimately does not occur, whether due to a regulatory decision, the outcomes of the risk/benefit assessment, or other factors.'** This should be worded so as to not place an undue burden on the investigators and reviewers at the early (discovery) stages of developing novel gene-drive systems. If a researcher has an idea about a novel approach and wants to determine first if it is feasible, they should not be required to provide a complete plan for what happens if it should work and advance to consideration for field release. If it does not function as planned in the preliminary laboratory work, then there is no need for articulating what happens downstream. However, I recognize the value of thinking in advance about how it might be used as this is likely to be informative in the design features of the novel system, and therefore some language to this effect should be included in the innovation and significance sections that accompany the early work. 3) **'5.4 Utilize an independent board to provide input on the assessments of potential benefits/harms, milestones, and any associated recommendations for potential field release studies.'** This is likely to be unworkable. How can this be set up practically, and who would pay for it? This was a criticism voiced previously to the Working Group and they have not provided a convincing plan or description of how this could be done completely free of actual or perceived conflicts-of-interest. It is imperative to explain how this will work. 4) **5.5 Make risk/benefit assessments publicly available, as well as any associated recommendations from the independent board, in a timely manner and to the greatest extent allowable by law.** This should be staged based on the success of the product development as it moves out of the discovery stages. Also, intellectual property controls will exempt some research creating two groups of researchers, those that are bound to this and those that are not. Both groups should be bound equally to this document. 5) **Section VI Strategies for Stakeholder Engagement**

	While there is consensus for the need for these activities, opinions on approaches vary, and what may be appropriate for one locale may not be for another. The relationship-based model proposed by Kormos *et al*.[i] should be acknowledged at least as it has been applied well in many aspects of health and medical sciences and practices. _____ [i]Kormos *et al*., (2020) Application of the relationship-based model to community and regulatory engagement for field trials of genetically-engineered mosquitoes for malaria control. *J. Am. Soc. Trop. Med. Hyg.* **104**:805-811. PMID: 33350374.

Submission # 2:

Date	6/22/2021
Name	Ethan Bier
Organization:	University of California, San Diego
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Comment:	Thank you for providing the opportunity to comment on the "**DRAFT Report of the Gene Drives in Biomedical Research Working Group**". I appreciate the thoughtful effort of the committee put into formulating this document. I have only a two general comments/suggestions to make in preparing the final version of this document. **1)** Although it seems clear from organization of the report that the criteria being applied to laboratory work versus field work will be different (sensibly so), I think it might be worth stating explicitly that the list of requirements for pursuing field studies including future plans for conducting risk assessments) should not apply to strictly laboratory work. I also am of the view that the safeguards outlined in the original NAS document on laboratory use of gene drives was well-conceived and that no scientific findings that I am aware of support increasing the stringency of physical or biological control measures in insects or mammals. I agree with the view that researchers planning to develop gene drives in other organisms should consult their IBCs prior to starting their work and that a uniform set of recommendations for insuring safe laboratory confinement of those systems is reasonable. One concern to keep in mind is that the greater the number of requirements that must be met before such work can be supported by the NIH, the fewer researchers may end up becoming engaged in this field thus limiting the diversity of scientific approaches to this important field. **2)** I very much agree with the recommendation that the NIH fund studies on mitigating strategies in the laboratory and that it should also support field studies. I believe, however, that it makes sense to be careful regarding when in the development timeline various milestone requirements need to be met. In accord with the view that each drive system should be considered on a case-by-case basis (a key principle in my opinion), I think it is best to leave sufficient flexibility in when various activities need to be accomplished or made public. For example, it would be a pity for a worthy project to be stalled due to overly proscriptive timelines on requirements such as when and by whom risk assessments are performed. Thank you again for providing an opportunity to comment on the NExTRAC draft document.

Submission #:3

Date	6/25/2021
Names:	Michael Santos
Organization:	Foundation for the National Institutes of Health
Email:	Public Comment Delivered Orally
Comment:	I'm Michael Santos, Acting Vice President for Science at the Foundation for the National Institutes of Health, and Director of the Gene Convene Global Collaborative. Gene Convene advances best practices and informed decision making for the development of genetic bio-controlled technologies, including gene drive, to improve public health. We want to recognize NIH, NExTRAC and the working group for taking this important step to operationalize the guiding principles for responsible gene drive research and thank you for the opportunity to provide feedback on the draft report. Many of the considerations described, such as the importance of appropriate expertise in biosafety review, stakeholder engagement, and data sharing are applications of principles that apply more broadly. The report should state which considerations are common to other areas and which are unique to gene drives. For contained research, recommendation 3.1 should be clarified to emphasize the importance of a risk-based approach to physical containment. As the current language on uniformed standards for physical containment facilities could be read as implying a one-size-fits-all approach. For field release, the plans recommended for inclusion in funding proposals reflect a set of important considerations for responsible research. However, these plans are likely to evolve after the proposal, and it is ultimately the implemented activities that support responsible research. In addition, the ongoing oversight of activities aligns more closely with regulatory and policy bodies than the NIH. Given that, the report should consider recommending that NIH defines its review in the context of a governance system that can include external advisory boards, IBCs, regulatory agencies, and local and national governments. Similarly, instead of requesting preliminary plans that may be difficult to evaluate, the NIH could require applicants to describe the governance mechanisms that will provide accountability for the research program. This approach would enable NIH to evaluate whether the governance system as a whole provides sufficient confidence that if the NIH funded the project, it would proceed responsibly consistent with existing policies and practices. Thank you very much.