

Genome Editing for Human Benefit: Ethics, Engagement and Governance

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Guidance and policy paper: Providing sound policy frameworks for responsible gene drive research: An analysis of the governance landscape and priority areas for further work

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Brief description of the context

Research on gene drive organisms is not new, but in recent years technical advances, such as CRISPR, have supported significant scientific advances, to the point where using gene drive organisms for tackling major issues, such as malaria, is now in the realm of the possible.^{1,2,3} The prospect of gene drive research moving from a laboratory-only setting to possibly being used to tackle public health and other issues “in the field” is now raising questions about the adequacy of the policy frameworks in place to responsibly manage and regulate the research and its outcomes.^{4,5,6}

Research and development of gene drive organisms in the laboratory has benefitted from extensive experience, peer-reviewed literature and well-established standards for managing biosafety and the integrity of research experiments.^{7,8,9,10} Many of these standards come from previous experiences with handling genetically modified organisms, such as crops, as well as much more complex and high-risk organisms, such as viruses. In addition, the institutions where research has primarily been taking place are part of national structures that provide oversight on biosafety, with institutional boards and permitting systems in place.

It is the next phase of research, for large ‘cage’ and field-based evaluations, where gene drive research has raised more questions. These areas are not without precedent – including genetically modified crops, Wolbachia-infected mosquitoes, and biological pest control – but nonetheless without an exact equivalent. Existing guidance, for example from the WHO’s [Guidance Framework for testing genetically modified mosquitoes](#) offer direction, and there have been recent efforts to develop guidance specific to gene drive organisms, such as the NASEM report “[Gene Drives on the Horizon](#)”, as well as recent publications, such as James *et al.* “[Pathway to Deployment of Gene Drive Mosquitoes](#)”^{11,12,13}.

Nonetheless, questions have been raised about how gene drive research can be conducted responsibly in these later stages of technology development and whether some of the specificities of gene drive organisms require additional or new frameworks to be developed. These questions arise in particular in the context of research taking place in Low and Middle-Income Countries (LMICs), which may not have the same experience in research with genetically modified organisms, and/or where gene drive organisms are intended to be evaluated for use.

The Outreach Network for Gene Drive Research brings together researchers and organisations working on gene drive research for public interest, organisations involved in outreach, stakeholder engagement and other relevant fields, as well as funders or supporters of these activities. Together members reach out to different stakeholders and provide expert views in policy fora where gene drive is discussed. The experience of the Network has shown that the topic of gene drive governance is broadly articulated around the following topics:

- Are international frameworks, such as the Convention on Biological Diversity’s Cartagena Protocol, relevant and adequate for gene drive organisms?

- Are national regulatory and policy frameworks in LMICs with limited or no prior experience of approving genetically modified organisms sufficient to ensure safe or responsible gene drive research?
- How are the communities in the field evaluations phases to be engaged? What would meaningful and legitimate community acceptance for field evaluations entail?
- Where should the power to make decisions about evaluations and use of gene drive organisms reside?
- Are there forms of gene drive or uses of gene drive which should not be allowed?
- How do different values, norms and visions of human relationship to nature shape the acceptability of using gene drive organisms, and how can different visions coexist?

Commentary, conclusion and recommendation

Discussions of governance and decision-making on gene drive should be examined through a layered system, where different forms and levels of governance and decision-making exist and build upon each other at international, national and local levels. They should also acknowledge that “gene drive” as a concept covers a broad range of approaches, which could result in organisms with very different characteristics and potential uses. As a result, seeking consistent and overarching answers to many questions may be unhelpful and misleading. That caveat should be at the forefront of these conversations and should in particular frame discussions about the desirability of using “gene drive” as broad category of organisms.

It is also important to recognise that conversations about gene drive are made more complex by the fact that they are intertwined in broader debates about the ethics of health research in low income settings, and the complex historical and cultural dynamics of ownership and leadership between Western countries and LMIC countries.

At the international level, the Convention on Biological Diversity is the main international framework dealing with genetically modified organisms. Gene drive organisms are broadly agreed to fall under its scope and so the provision of the CBD and its Protocols are applicable, including on topics such as transboundary movement.¹⁴ But the international system is based on individual sovereign states, so the crux of implementation and decision-making falls to countries. Their ability to build and implement the appropriate legal frameworks to evaluate gene drive organisms and manage their release is crucial to responsible research.

Not all countries have put in place national biosafety laws and the attendant processes to evaluate and monitor genetically modified organisms. Some may have the laws but no prior experience in applying them. The concept of leveraging gene drive approaches to address public health and conservation issues is novel to every country, so to some degree the question of experience maybe moot. Yet, it is reasonable to assume that experience in managing other genetically modified organisms is useful since gene drive organisms are also genetically modified organisms. This experience is available, and those who have not had it can learn from others. There are efforts to encourage regional-level experience sharing and capacity building (for example between countries in the ECOWAS region), as well as exchanges between countries (for example between African nations and Brazil) and other support through the Convention on Biological Diversity.

While states are the recognised decision-making unit in the international system, there are also provisions in international law and in many national legislations, supported by growing public consensus, for local communities to be involved in governance and decision-making.^{15,16,17} Community engagement is not a new concept and not exclusive to the use of gene drive organisms. It is widely incorporated in many fields, from public health to infrastructure development to extractives. These experiences are useful, but it is likely that there is no one-size-fits all model or approach for community engagement on gene drive research that can be applied everywhere. There is great diversity in the social, historical and cultural contexts in which gene drive research may take place. Working with the concerned communities themselves in shaping how they want to be engaged and make decisions is more likely to yield meaningful engagement and acceptance than seeking a monolithic model of engagement to be applied across all research.¹⁸

As research on gene drive progresses, all the actors involved in its development, management and regulation are thinking through the issues raised in this paper. Some of these questions may not ever be fully resolved and will always see divergent perspectives. However, acknowledging the issues, and where possible, outlining processes or frameworks to allow researchers and other stakeholders to consider them in a case-by-case and systematic way, is essential to ensure research is carried out responsibly.

References

1. WHO Strategic Advisory Group on Malaria Eradication (2019) Malaria eradication: benefits, future scenarios and feasibility. Executive summary - <https://www.who.int/publications-detail/strategic-advisory-group-malaria-eradication-executive-summary>
2. Richard G. A. Feachem, *et al.*, (2019) Malaria eradication within a generation: ambitious, achievable, and necessary. *The Lancet*. Volume 394, Issue 10203, pp. 1056-1112, [https://doi.org/10.1016/S0140-6736\(19\)31139-0](https://doi.org/10.1016/S0140-6736(19)31139-0).
3. ICUN (2019) Genetic frontiers for conservation: an assessment of synthetic biology and biodiversity conservation: synthesis and key messages. <https://doi.org/10.2305/IUCN.CH.2019.04.en>
4. Evans, S. W., and Palmer, M. J. (2017). "Anomaly Handling and the Politics of Gene Drives." *Journal of Responsible Innovation* 5 (S1): S223–S242; <https://www.tandfonline.com/doi/full/10.1080/23299460.2017.1407911?scroll=top&needAccess=true>
5. Kuzma, J., F. Gould, Z. Brown, J. Collins, J. Delborne, E. Frow, K. Esvelt, *et al.* (2017). "A Roadmap for Gene Drives: Using Institutional Analysis and Development to Frame Research Needs and Governance in a Systems Context." *Journal of Responsible Innovation* 5 (S1): S13–S39; <https://www.tandfonline.com/doi/full/10.1080/23299460.2017.1410344>
6. James *et al.* (2018). "Pathway to Deployment of Gene Drive Mosquitoes as a Potential Biocontrol Tool for Elimination of Malaria in Sub-Saharan Africa: Recommendations of a Scientific Working Group". *American Journal of Tropical Medicine and Hygiene*. Volume 98, Issue 6_ Suppl 2018; <https://doi.org/10.4269/ajtmh.18-0083>
7. Benedict, *et al.*, (2018) Guidance for Contained Field Trials of Vector Mosquitoes Engineered to Contain a Gene Drive System: Recommendations of a Scientific Working Group. *Vector-Borne and Zoonotic Diseases*, 8:127. <https://doi.org/10.1089/vbz.2017.2121>
8. Akbari *et al.*, (2015) [Safeguarding Gene Drive Experiments in the Laboratory](https://doi.org/10.1126/science.1270000). *Science* 349:927
9. Stephen Higgs, *et al.* (2004) [Arthropod Containment Guidelines](https://doi.org/10.1186/14752875). 2004 Vector Borne Zoonotic Dis. 3:61. <https://doi.org/10.1089/153036603322163439>
10. Roberts A., Paes, de Andrade, P., Okumu F, *et al.* (2017) [Results from the Workshop "Problem Formulation for the Use of Gene Drive in Mosquitoes"](https://doi.org/10.1186/s12928-017-0333-3). *Am. J. Trop. Med. Hyg.* 96(3):530–533
11. WHO (2014) Guidance Framework for Testing of Genetically Modified Mosquitoes. <https://www.who.int/tdr/publications/year/2014/guide-fmrk-gm-mosquit/en/>
12. National Academy of Sciences, Engineering and Medicine (2016) [Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values](https://doi.org/10.17232/amn.2016.11001) 1st ed. Washington DC: The National Academies Press; 2016.
13. James, S. *et al.* (2018) (*ibid.*)
14. Ad hoc Expert Group on Synthetic Biology (2017) [Report of the AHTEG](https://doi.org/10.1017/S1446758117000013). CBD/SYNBIO/AHTEG/2017/1/3
15. National Academies of Sciences, Engineering, and Medicine (2016) (*ibid.*)
16. Kolopack PA, Lavery JV. (2017) Informed consent in field trials of gene-drive mosquitoes. *Gates Open Res.* 1: 14. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5757819/>.
17. Lavery JM, Tindana PO, Scott TW, Harrington LC, Ramsey JM, Ytuarte-Nunez C, *et al.* (2010) Towards a framework for community engagement in global health research.

Trends Parasitol. 26(6): 279-283.

<http://www.sciencedirect.com/science/article/pii/S1471492210000425?via%3Dihub>.

18. Thizy D, Emerson C, Gibbs J, Hartley S, Kipiriri L, *et al.* (2019) Guidance on stakeholder engagement practices to inform the development of area-wide vector control methods. PLOS Neglected Tropical Diseases 13(4): e0007286. <https://doi.org/10.1371/journal.pntd.0007286>