Gene Drive Research Forum 2022 Report

Co-hosts: McMaster University Institute on Ethics & Policy for Innovation (IEPI) and GeneConvene Global Collaborative

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Location: Le Châtelain Hotel, Brussels, Belgium

The 2022 meeting of the Gene Drive Research Forum took place this November in Brussels over a period of two days, marking the fifth anniversary of the publication of the Principles for Gene Drive Research. The meeting brought together researchers, funders, representatives of regulatory authorities, stakeholder engagement experts, and other stakeholders interested in gene drive research, to take stock of the progress made over the last five years to operationalize these principles. The meeting also provided an opportunity for constituents to discuss how the Forum could help inform, guide, and support gene drive research and what should be its priorities going forward.

Day one focused on progress in advancing the five Principles for Gene Drive Research and featured presentations from experts in the field, followed by moderated open discussions, while day two was devoted to forward-looking discussions about the future of the Forum.

Principle 1: Advance quality science to promote the public good

Discussions of the first session began with an overview of various gene drive applications and how these could deliver public good, whether in public health, conservation, or agriculture. This was followed by an exploration of the scientific progress made in recent years, including the robust advances in developing both the theoretical and conceptual landscape of approaches for several gene drive applications, as well as proof of principle in multiple organisms. Presenters also stressed that researchers had been working to develop various mechanisms to address concerns about safety and control, as well as building knowledge and practice in stakeholder engagement to support responsible research. As part of the discussions, the development of gene drive approaches for population replacement - including in other organisms than Anopheles mosquitoes, was cited as recent progress, as well as the possibility for field testing separate components of a gene drive system without releasing fully driving organisms. Additionally, the recent promising development of a world-first proof of concept for the control of invasive mice using t-CRISPR was noted.

Overall, panelists agreed that while research has progressed to be able to deliver on the promise of gene drive tools for the public good, the pathway from laboratory success to public good is a long and complex one and there are still challenges to overcome, including issues such as those related to transboundary movement. The potential to develop a sort of "safety switch" for stopping the progression of gene drive spread was discussed. Panelists also acknowledged the need for more capacity-building initiatives, to adopt a case-by-case approach, and to understand what types of data will be required for regulators. Panelists also underlined the value of investing in laboratory work of different gene drive constructs as well as the importance of outreach and communications about the technology.

Principles 2 & 3: Promote Stewardship, Safety, and Good Governance, & Demonstrate Transparency and Accountability

The second session of the day took the form of presentations and began with a presentation on the World Health Organization's perspectives on the use of genetically modified mosquitoes to control vector-borne diseases, reminding participants that population suppression and modification approaches are not novel approaches, but rather share similarities with the Wolbachia and the Sterile Insect Technique (SIT) approaches. The next presentation offered a look at the progress in developing guidance to support the responsible development of gene drive organisms under the Convention of Biological Diversity, and touched on the effectiveness of the Cartagena protocol, reminding audiences that only 55% of parties have fully introduced measures to implement biosafety protocols, and emphasizing the need for capacity-building resources. The presentation that followed provided an overview of the European Food Safety Authority's guidelines for the risk assessment of genetically modified insects. Although a review found these are adequate, it was recommended that further guidance is needed for certain aspects of risk assessment of gene drive modified insects. The speaker also noted that modelling will play a key role in helping identify potential risks. The following presentation recalled the work done through the Forum to date on governance, transparency and accountability. The presenter advised that the gene drive community should consider mapping existing governance frameworks relevant to gene drives and suggested that a stronger focus going forward on the implementation of the principle of accountability. The last intervention was a recorded presentation which shed light on AUDA-NEPAD led efforts in the African region to build capacity and preparedness for gene drive development for malaria vector control.

The third session was a moderated open discussion in which several key questions were raised:

- Who should be responsible for governance mapping?
- How can projects learn from each other's regulatory journeys? Is there a role for the World Health Organisation to help avoid replication on a country-by-country basis?
- What is the relationship between trust and accountability?
- What should communication to stakeholders entail?
- Is doing what is required legally enough or should researchers go above and beyond what may be required legally? What additional activities might be helpful or necessary?
- Should elements of Principles 1, 2 and 3 be updated now that there are more concrete examples to draw from?

Principles 4 & 5: Engage Thoughtfully with Affected Communities, Stakeholders, and Publics & Foster Opportunities to Strengthen Capacity and Education

Session 4 began with a presentation on the University of California Malaria Initiative's progress in applying the relationship-based model for stakeholder and community engagement in Sao Tome and Principe, where UCMI has been working since 2019. The presenter explained that, for each phase/ stage of research, the engagement team develops a specific engagement plan for each identified stakeholder group and emphasized that the development of trust and collaboration between different parties

involved are at the core of UCMI's stakeholder engagement strategy. The presentation that followed gave audiences an overview of Target Malaria's updated community agreement model, which builds on the project's previous approach, whilst taking into consideration lessons learned in the course of its field research to date. The speaker described the project's efforts to review the issue of community agreement and its approach as it enters its next phase of technology development, the potential release of genetically modified male bias mosquitoes. This was followed by a recorded presentation of the findings of a report by The Commonwealth Scientific and Industrial Research Organisation (CSIRO), exploring the Australian public's attitudes and perceptions towards the use of gene drive technology for the management of invasive species. Results of the study showed that a majority of participants are supportive of the development of gene drive technologies to control invasive populations of feral cats. Those unsupportive of the development of the technology tended to cite previous failed attempts at controlling invasive alien species populations, while the supportive survey participants focused on the urgency of finding solutions to current biodiversity challenges. The fourth presentation provided an overview of the African Genetics Biocontrol Consortium & GeneConvene's capacity-building projects, including informational webinars and intensive workshops on aspects of biosafety training. The African Genetic Biocontrol Consortium is a group of member organisations whose vision is to expand African self-determination of the course of research, development, and use of genetic biocontrol approaches for public health and conservation. The session concluded with a presentation on the efforts of the Pan-Africa Mosquito Control Association (PAMCA) to build capacity and provide opportunities for education around gene drive research. The speaker explained the formation of the African Gene Drive for Vector Control Network with the main objectives of creating a platform for networking, knowledge sharing, regional collaboration and cooperation; establishing a community of practice; promoting collaboration across the African continent; and promoting the next generation of African-led research. The establishment of "gene drive trainings" to build understanding of gene drive technologies among professionals from different backgrounds was also highlighted.

The fifth session consisted of a moderated open discussion that expanded on questions of engagement and capacity strengthening, including:

- Who is responsible for stakeholder engagement? Is it only the responsibility of stakeholder engagement teams or all members of the project?
- How can stakeholder engagement practitioners working on gene drive engagement collaborate to share knowledge and best practices?
- How do we define a standard for community agreement to be legitimate, taking into consideration best practices from different projects and context-dependent issues of legitimacy and credibility?

Key recommendations made in the fifth session:

- Development of a stakeholder engagement approach for gene drive research should follow an iterative approach, allowing for the integration of learnings along the development pathway of gene drive technologies.

- More opportunities for capacity building in gene drive research should be created, such as offering of fellowships or PhD opportunities for interested individuals from countries where the technology may be tested or applied.

Key themes from forward-looking discussions:

Day two began with session six, which took the form of an informal panel discussion to reflect on the areas where more progress is needed and explore how the challenges identified in in the previous day's discussions can be addressed moving forward. Some of the challenges mentioned by session six panelists included:

- Understanding what it would take to implement public health tools and understanding the needs of end users;
- Identifying the characteristics of a minimum acceptable product;
- Considering potential challenges in the area of operational research, which could be different for self-sustaining and self-limiting technologies;
- Encouraging more researchers to go from academia to implementation;
- Consolidating learnings and approaches developed by different projects and identifying opportunities to apply them across different projects to increase efficiency and consistency;
- Considering how to support modelling of gene drive technologies by experts independent from projects, to offer corroboration and increase confidence in findings;
- Continuing to refine mechanisms for stakeholder engagement, recognizing that it is an integral part of building science;
- Engaging thoughtfully by distinguishing between outreach and engagement, considering the role of engagement in each phase of technology development, respecting and understanding the social, legal and regional political context for obtaining consent to conduct research, and considering procedural justice.

When asked in which areas they would most like to see advancements in the next five years, panelists mentioned they would like to see more capacity strengthening and co-development models, as well the creation of other groups modelled on this forum for different types of synthetic biology applications. One panelist mentioned that in five years, we might realize that the work done under the Forum has contributed to the readiness level not only for gene drive but for other advanced technologies.

Key priority areas:

Session seven consisted of roundtable discussions to reflect on the previous day's summaries and progress reports and to yield concrete suggestions of actions and areas of work that can be discussed further in the final session. Forum participants were divided into breakout rooms and were given different questions to reflect on. The questions revolved around six key themes from day one: mapping the governance landscape, building trust and accountability, deciding when a gene drive product is

"good enough" to move to field testing, preparing the way for field evaluations, pinpointing where gene drive is unique, and building efficiencies of scale.

The final session of the day, session eight, took the form of a plenary discussion to propose the key priority areas for the Forum going forward. The key recommendations outlined in the discussion included involving a broader range of stakeholders in the Forum, including end users, as well as developing ways to coordinate and consolidate knowledge obtained through the experience of different projects in a way that could be useful to all stakeholders. Coordination of modelling and communications activities were of particular interest. Participants also agreed that the mapping of relevant governance frameworks could be a useful starting point to help prioritize future actions.

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