OUTREACH NETWORK FOR
GENE DRIVE RESEARCH

Annex II
Template for submitting information on additional trends and issues that were identified and prioritized by the multidisciplinary AHTEG for information gathering

Part I. Endorsement of submission
Name of Country/Organization: Outreach Network for Gene Drive Research
Name of CBD National Focal point/Head of Organization endorsing: Isabelle Coche
Signature of the CBD National Focal Point/ Head of Organization:
Date: November 24, 2023

Part II. Submission of information
In submitting information, kindly provide the following information on one or more of the 12 trends and issues in synthetic biology as follows:

1. Trend and issue in synthetic biology chosen
2. Potential positive and potential negative impacts on the three objectives of the Convention
   a. Conservation of biological diversity
   b. Sustainable use of its components
   c. Fair and equitable sharing of the benefits arising out of the utilization of genetic resources
3. Potential gaps or challenges for risk assessment, risk management and regulation, including availability of tools for detection, identification and monitoring
4. Additional relevant considerations (e.g., socioeconomic, ethical, cultural, human health, intellectual property, liability and redress, IPLCs, public engagement, among others)
5. Timeframe to commercialization or release into the environment
6. Potential linkages to the Kunming-Montreal Global Biodiversity Framework and potential contribution to other internationally relevant goals and targets

Submission of supporting documentation:

For any publication that you may want to share as part of your submission, kindly include:

1. Name of publication(s), author, date and DOI or URL link.
2. Attach in pdf format any publication you have listed above.

Please note that this submission is restricted to aspects relevant to gene drive and not broadly for all synthetic biology.

5. Use of synthetic biology in wild organisms in the context of resilience in threatened species

Over the past two decades, the number of endangered species and the rate of ecosystem degradation have increased dramatically across all regions. While many successful initiatives have helped protect biodiversity and support healthy ecosystems, issues of cost, replicability, and scalability have limited the capacity of existing methods to fully address current environmental challenges. New technologies, such as those based on synthetic biology, could make significant contributions to reverse these trends in biodiversity loss.

There are several promising areas of research underway. For example, scientists are currently considering genetic engineering and gene editing tools to enhance coral's thermal stress tolerance in response to climate change and ocean acidification. Researchers have also produced American chestnut trees that resist infections due to an invasive blight fungus, potentially saving the species from extinction. Synthetic biology is also under consideration to protect endangered native birds from avian malaria, for example in Hawai'i. Last year, researchers created a proof of concept for a gene drive mouse, which could help control invasive mice populations in certain ecosystems – one of the most common invasive alien species and main drivers of species extinctions on islands.

Synthetic biology tools must comply with existing legislation and regulations, following a rigorous risk assessment process to assess possible risks to the environment and human health. The decision on whether to develop and implement these tools must be based on science and the case-by-case approach, considering their benefits and risks, and comparing those to the impact of existing alternative tools.

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9. Interaction of synthetic biology organisms in the environment and potential for cumulative effects

How relevant the issue of interaction of different synthetic biology organisms in the environment is depends on many factors – for example, whether the organisms in question belong to the same species, are in the same space (region, country, etc). For gene drive LMOs, the risk assessment process should and would consider the "receiving environment" in which the gene drive LMO is proposed to be released. If that environment includes other gene drive organisms of relevance, then possible interactions should and would be taken into account, in the same way that interactions and impacts on other relevant species and organisms in the receiving environment are. In the case of a gene drive malaria mosquito, if that mosquito were to be released in a country where a prior release of a different gene drive mosquito had taken place, the risk assessment should and would consider this interaction, in the same way that it would consider the possible impact of the mosquito on other wild mosquito species and other organisms (in the food chain for example).

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10. Dual-use nature and biosecurity implications of synthetic biology

Gene drive organisms are considered to present a low risk profile for dual use due to their characteristics. Gene drives work only with sexually reproducing organisms, such as animals (including insects) and most plants, but not viruses or bacteria. The latter are generally considered the primary opportunities for potential bioterrorism. Rather than attempting to modify plants or animals directly, it is much more likely that a potential bioterrorist would target a pathogen of the organism of interest. In order to produce rapid effects, gene drives also require species with a short reproductive cycle, which further reduces their applicability. Finally, the novelty of "gene drive" is in the fact that it allows a modification to become established in a population over time, but the type of modification (for example reducing fertility) is no different from the type of modification that can be created through "classic" (non gene drive) genetic modification.

In addition to the technical aspects, it is important to consider that the development of gene drives is expensive, complex, lengthy, and requires a high level of technical expertise. It is not a technology that could be easily and quickly developed in "home" laboratories by a small team, or easily applied to a wide range of species. Even with the increasing use of CRISPR in several research fields, including gene editing research for agriculture, conservation, or human health, creating a gene drive organism is neither easy nor quick. Understanding what modification may be effective and where it could be placed requires special expertise to ensure the modification is stable and has the desired effect over time.

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11. Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products

Transboundary movement is a relevant consideration for gene drive organisms, as LMOs containing gene drives would be able to move of their own accord, adding another layer of complexity in terms of managing the movement compared to, for example, LMO crops. Any release of gene drives for research and application purposes is subject to approval by national regulatory agencies, which would consider the movement of modified organisms across borders (transboundary movement) as an integral part of their assessments.

Discussions are already ongoing about how joint dossier review or other mechanisms could be put in place to ensure the release of gene drive, and their potential to cross national borders, is carried out with neighbouring countries' assent and in compliance with biosafety regulations. African governments, for example, have been discussing how to manage possible future releases of gene drive mosquitoes for some time. The 2018 African Union report on gene drive concluded that "because of the potential for transboundary movement, decision-making on the implementation of gene drive mosquitoes will need to take place in a regional context." In West Africa, where research is most advanced, African officials have established the Integrated Vector Management Platform and prepared joint guidelines on how to evaluate any request for research on gene drive mosquitoes through that platform to manage vector control tools, including gene drives. Discussions are ongoing about scaling that platform to the whole Africa region. The Cartagena Protocol also allows for countries to adopt additional measures to address transboundary movements at the national level if they feel it is required, as long as they are in keeping with their international obligations.

In addition to regulatory oversight of any release, detection and identification are important considerations for both experimental field releases (for research purposes) as well as for possible use of gene drive LMOs to control vector-borne diseases or invasive alien species in the future. The current discussion on detection and identification methods and whether gene drive LMOs would require new techniques or tools have largely noted that gene drive organisms do not generally present significant or substantive challenges for detection and identification compared to other LMOs. However, there are some aspects to consider that could be addressed through collaborations of expert centers, such as establishing validated methods for detection and identification that can be used in very different organisms, and establishing the appropriate identifiers, sampling strategies and detection limits, among others.

The capacity to detect and identify LMOs is core to the ability to monitor and maintain biosafety and underpins the implementation of the provisions of the Cartagena Protocol. It is not the novelty of the traits or methods that is a challenge, but the capacity, information and access to facilities that can challenge a country's ability to detect and monitor. More investment to improve access to laboratories, to share knowledge, build capacity on detection methods, and share information about LMOs should be a priority.

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12. Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder

No field evaluations of gene drive organisms have been conducted to date. However, there have been a small number of field evaluations of genetically modified insects in several countries, all of which have been approved by national authorities. The nationality of the

developer or funder is irrelevant to the choice of location for a field evaluation, which should take place in the location of intended use. All field tests of synthetic biology organisms will be subject to the approval of national authorities and the applicants will take responsibility for damage to the environment and impacts, as set out in national legislation of the country where the field evaluation takes place, regardless of where the applicants are based.

As noted in guidelines on gene drive research (for example, WHO 2018), field evaluations provide invaluable data and are essential in supplying evidence on the efficacy of proposed applications of gene drives in real-world conditions. A risk assessment will need to be conducted to ensure that the release does not pose unacceptable risks and to determine what the negative and positive impacts on human and animal health and the environment could be. In preparation for this stage of the research, scientists and national authorities can rely on the results of studies conducted in laboratory settings and virtual modelling and draw on prior experience in agriculture, pest biocontrol, public health, and other fields, as well as guidance from authorities such as the WHO. Building national capacity in areas such as ecology, entomology, molecular biology, regulation and others to enable an effective and safe design and implementation of field evaluations is essential.

It is worth noting that a significant part of the research is taking place in countries where the tool would be implemented, such as in several countries in Africa where malaria is endemic and in Australia where invasive alien mice are a major concern. For example, institutions in Uganda and Burkina Faso are members of Target Malaria – a not-for-profit research consortium that aims to develop genetic technologies to modify mosquitoes and reduce malaria transmission – and are core to the development of the technology, from laboratory experiments to field entomology and regulatory approvals for their work. Similarly, Transmission Zero is an international research programme that brings together scientists of the Ifakara Health Institute, the National Institute of Medical Research in Tanzania and Imperial College London in the UK to work on gene drive tools for eliminating malaria transmission. Another example is the University of Adelaide, part of the GBIRd Partnership, which announced in 2022 the world's first proof of concept of gene drive technology to control invasive mice, a major threat to biodiversity in Australia.

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