International policy framework for genetically modified mosquitoes

Target Malaria is a not-for-profit research consortium, working to develop a sustainable and cost-effective tool for malaria control, using genetically modified mosquitoes. Genetically modified organisms (GMOs) are highly regulated in most countries. National laws and structures are used to regulate and manage GMOs, and they reflect the commitments each country makes under international agreements.

The innovative genetically modified mosquitoes that we are developing use gene drive technology. This technology allows a genetic modification to bias its own inheritance and to spread through a target population at an increased frequency, compared to a non gene drive modification. As our mosquitoes are genetically modified, the regulations for GMOs apply.

To date, environmental releases of genetically modified insects in various countries in the world (in some cases at a very large scale) have been non gene drive strains, meaning that if the releases stop, the modifications disappear from the local insect population within a relatively short timeframe. Release of mosquitoes with our gene drive technology would be different as the intention would be for the modification to persist in and reduce mosquito populations over a longer timeframe in the immediate area of release and also to spread and reduce other neighbouring populations. This ability to spread and persist (albeit in much reduced populations) is the basis for the much higher efficiency of gene drive compared to non-drive approaches, and raises new questions and challenges for regulators as a first in class intervention.

Regulatory compliance is a core pillar for Target Malaria. Our dedicated regulatory team are tasked with ensuring that Target Malaria is compliant with current regulations, relevant international treaties, and national laws. The regulatory team are responsible for anticipating how national policies may affect our development pathway for a tool for mosquito control based on gene drive and adjusting our strategies to be compliant.

We highlight below global and regional organizations that are responsible for key policy instruments in the governance of gene drive research.

The Convention on Biological Diversity (CBD)

The main international policy framework that addresses the use of GMOs is the United Nations Convention on Biological Diversity (CBD). The CBD entered into force on 29th December 1993 and has three main objectives:

1. The conservation of biological diversity
2. The sustainable use of the components of biological diversity
3. The fair and equitable sharing of the benefits arising out of the utilization of genetic resources

The Convention has almost global participation, with 196 countries as Parties to the Convention. The text of the Convention includes an obligation to regulate, manage or control GMOs defined in the text as **Living Modified Organisms (LMOs)**, that may have an adverse effect on biodiversity (Article 8(g)). It also includes a legal basis for a Protocol setting out the safe transfer, handling and use of any LMO resulting from biotechnology where required (Article 19(3)). Gene drive organisms are classified as LMO's under the CBD and its protocols.

On 29th January 2000, the Conference of the Parties to the CBD adopted a supplementary agreement to the Convention known as the **Cartagena Protocol on Biosafety**[1]. The Cartagena Protocol establishes procedures for the safe transfer, handling and use of LMOs and also provides a risk assessment framework for LMOs (Annex III). **173 countries** are Parties to this protocol, **including all of the African countries where Target Malaria currently works**[2]. A supplementary protocol to the Cartagena Protocol came into force in March 2018: the **Nagoya – Kuala Lumpur Supplementary Protocol on liability and redress**, to specify measures to be taken in the event of damage to biodiversity resulting from LMOs, and also includes provisions in relation to civil liability.

A further protocol under the CBD is the **Nagoya Protocol** that governs the access and benefit sharing of genetic resources.

At COP-MOP11of the Cartegena Protocol, parties welcomed the adoption of Additional Voluntary Guidance Materials for the Risk Assessment of Living Modified Organisms containing Engineered Gene Drives. These guidelines had been formulated over the previous year by a group of experts; they are science-based and support case-by-caseassessments of gene drives in line with CBD and international best practices.

World Health Organisation (WHO)

The World Health Organization (WHO) is the United Nations agency responsible for global public health. As malaria is one of the greatest global health problems, with over 600,000 deaths and 200 million cases a year, WHO has a large programme of work around this disease. The World Malaria Programme includes tracking and reporting data and statistics on malaria cases (World Malaria Report) and monitoring developments that may advance or harm progress in malaria elimination. WHO assesses new tools for malaria control, such as insecticides and vaccines, using an evidence–based framework.

Tools for vector control pass through three WHO processes:

- Malaria Policy Advisory Group (MPAG) gives policy recommendations for all tools;
- Vector Control Advisory Group (VCAG) assesses public health value for novel vector control tools, based on epidemiological evidence
- Prequalification team for vector control (PQT-VC) assesses the safety, quality and efficacy of new tools.

Gene drive mosquitoes would most likely be assessed using the same processes as other vector control tools.

WHO has historically taken a lead, as early as 1991, in the discussions regarding genetic modification of insects that are vectors of human diseases, by hosting discussions and expert fora and initiating training courses. WHO has publicly welcomed the development of innovative vector control tools including gene drive mosquitoes through its Position Statement on the evaluation and use of genetically modified mosquitoes (GMMs) for the control of vector-borne diseases (VBDs), and in 2021 issued an updated 'Guidance Framework For Testing Genetically Modified Mosquitoes' to encourage 'informed and rigorous evaluation by researchers, developers, those responsible for regulatory and policy decisions and the people to whom these stakeholders are accountable'.

African Union Development Agency-New Partnership for Africa's Development (AUDA-NEPAD)

The African Union Development Agency-New Partnership for Africa's Development (AUDA-NEPAD) is an economic development program of the African Union. AUDA-NEPAD aims to provide an overarching vision and policy framework for accelerating economic co-operation and integration among African countries.

In 2017, the African Union (AU) High-Level Panel on Emerging Technologies (APET) recommended that gene drives be thoroughly examined as a realistic option for effective malaria control and elimination as part of existing integrated vector management (IVM) (AUDA-NEPAD, 2017). Following this recommendation, African Ministers of Science and Technology (Assembly of the African Union, 2017) and the African Union Executive Council (Executive Council Thirty-Second Ordinary Session, 2018) also recommended African Union member states **consider gene drive insects in their development plans.** The 2nd APET report on Gene Drives for Malaria Elimination in Africa was published in February 2025.

AUDA-NEPAD has worked with the West Africa Health Organization (WAHO) to establish an AU-recognized regional IVM platform aligned with ECOWAS member states to implement these AU resolutions. The resulting **West Africa IVM platform** (WA-IVM) includes health and environment regulators, ethics committee members, and malaria control program managers from Burkina Faso, Côte d'Ivoire, Ghana, Mali, Nigeria and Senegal in a **One Health**, multisectoral regional governance approach for vector control and elimination.

Other key organizations

Commonwealth Scientific and Industrial Research Organisation (CSIRO)
The Commonwealth Scientific and Industrial Research Organisation (CSIRO) is an Australian Government agency responsible for scientific research. Their Data 61 Ecological and Environmental Risk Assessment (DEERA) team are leading the implementation of probabilistic risk assessments for genetically modified mosquitoes and for gene drive mammals.

European Food Safety Agency (EFSA)
The European Food Safety Agency (EFSA) is the agency of the European Union (EU) that provides independent scientific advice and communicates on existing and emerging risks associated with the food chain. They are a key authority in scientific guidance to European policy for LMOs.

In 2020, EFSA published a report, at the request of the EU Commission, assessing whether their current guidelines for the risk assessment of genetically modified animals (EFSA, 2012 and 2013), including insects, was adequate for organisms containing an engineered gene drive. They concluded that the current framework was largely sufficient, but that additional guidelines could be needed in some areas, such as persistence and invasiveness, use of modelling, and molecular tools for detection.

The International Union for Conservation of Nature (IUCN)
The International Union for Conservation of Nature has a membership of over 1400 governmental and non-governmental organisations working in the field of nature conservation and sustainable use of natural resources. IUCN has observer and consultative status at the United Nations and plays a role in the implementation of several international conventions on nature conservation and biodiversity, including the CBD. At the IUCN World Conservation Congress in 2016, Resolution 6.086 was adopted, entitled "Development of IUCN policy on biodiversity conservation and synthetic biology", to examine the impacts of the production and use of the products resulting from synthetic biology including engineered gene drives on the conservation and sustainable use of biodiversity, to recommend how IUCN could engage in ongoing discussions and deliberations with the synthetic biology community and to develop guidance on the topic. This led to the formation of a task force and technical subgroup, and the publication of a

technical assessment in 2019, "Genetic Frontiers for Conservation", but an official IUCN policy was not formally adopted. Since then, a further resolution "Towards the development of a IUCN policy on synthetic biology in relation to nature conservation" was made in 2019; the policy is still in development.

National Academies of Sciences, Engineering and Medicine (NASEM)
The National Academies of Sciences, Engineering and Medicine (NASEM) are the United States non-profit, non-governmental organisations charged with 'providing independent, objective advice on matters related to science and technology'.

In 2016, they produced a publication entitled 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values' outlining the state of knowledge at that time relative to the science, ethics, public engagement, and risk assessment for research on gene drive, and governance of the research process. The report offered principles for responsible practices of gene drive research and related applications for use by investigators, their institutions, the research funders, and regulators.

Organisation of Economic Development and Co-operation (OECD)
The Organization for Economic Development and Co-operation (OECD) is an international economic non-governmental organisation with a membership of 38 countries. The majority of OECD members are high income countries. The organization's mission is to provide a forum and knowledge hub for data and analysis, exchange of experiences, best-practice sharing, and advice on public policies and international standard-setting.

In 1995 OECD established a **working group for harmonisation of regulatory oversight in biotechnology** to improve mutual understanding and harmonised practice in biosafety evaluation, including methods of evaluation for regulatory/ risk assessment of LMOs. They have produced 68 science-based consensus documents widely used by regulators, including 'Safety Assessment of Transgenic Organisms in the Environment Volume 8' on the biology of *Aedes aegypti* mosquitoes. A similar document for *Anopheles gambiae* is in development.

The above gives an outline of an evolving policy landscape for the responsible management of living modified organisms containing an engineered gene drive. In addition to the organisations above, many reports have already been published (and more will undoubtably be added in the future) by independent scientists and ethicists, to offer a framework for responsible gene drive research, and to help guide decision makers.

1. *The Cartagena Protocol came into force in September 2003*
2. *The United States has signed but not ratified the CBD*