Draft Outline of the Guidance Document on LM Mosquitoes

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The Parties to the Cartagen Protocol have mandated the AHTEG to prioritize the identified needs for further guidance on risk assessment and risk management. A sub-working group on LM Mosquitoes (SWG-LMM) was formed to produce modalities for development of guidance documents on risk assessment and risk management of living modified mosquitoes.

In the context of the steps contained in paragraph 8 of Annex III of the Protocol, the general structure of this guidance document should be organized by providing: (i) points to consider; (ii) rationales for the points to consider; and (iii) relevant bibliographies and supporting documents.

INTRODUCTION

Living modified (LM) mosquitoes are being developed for use to reduce transmission of vector borne human diseases, especially malaria and dengue. Various strategies are being developed to control the population of vectors by suppressing their population or reducing their vector competence.

The biology and ecology of mosquitoes, and their importance to public health as vectors of human disease and morbidity pose new considerations to the risk assessment and risk management of LMOs, which has been based mainly until the present on the existing experience with LM crop plants. .

The lack of a clear regulatory framework in many countries, lack of guidance documents, other than public environmental impact assessments done on LM fruit fly agricultural pests, and lack of experience in regulatory agencies to handle the deployment of recombinant DNA strategies to combat vector related diseases creates challenges. The technical requirements for efficacy, environment and health impacts need to be taken into consideration. While the various approaches to combat vector borne diseases using LMM may have many issues in common, it is recognized that there may be different sets of challenges to address the specific strategies.

This is intended to be a living guidance document that will be shaped and improved with time, as new experience becomes available and new developments in the field of applications of LMOs occur, as and when mandated by COPMOP.

OBJECTIVE

The aim of this document is to complement the road map[1] as well as provide additional relevant information that can contribute to the understanding of the subject and help regulators in their decision-making process in relation to the environmental release of Living Modified Mosquitoes.

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[1] The Parties to the Cartagena Protocol on Biosafety (the Protocol) have mandated the AHTEG to 'develop a "roadmap", such as a flowchart, on the necessary steps to conduct a risk assessment in accordance with Annex III to the Protocol and, for each of these steps, provide examples of relevant guidance documents'. Annex III constitutes the basis of the roadmap.

SCOPE

Many countries face great public health challenges due to mosquito-borne diseases such as malaria, dengue, chikungunya and yellow fever. This document will focus on LM mosquitoes developed for use in vector control of human diseases.

POINTS TO CONSIDER

a) Biological diversity (species and ecosystem) effects

Rationale
The release of LM mosquitoes may have a negative impact on the target and other species.

Topics to consider:

- What is the impact on the target mosquitoes?
- May the LM mosquitoes have an adverse effect on other species becoming agricultural, aquacultural, public health, or environmental pests or develop nuisance or health hazards?
- What is the habitat range of the species?
- Is the species native / invasive in a given area?
- Will the release affect mosquitoes species that are pollinators of agricultural crops?
- What species do the target mosquitoes typically interact with in the environment?

Based on the existing knowledge on the ecology and biology of mosquito species that transmit malaria and dengue, it may not be likely that other species will be affected by LM mosquitoes. More information is needed in cases involving other mosquito species and some environments where the LM mosquitoes are likely to be released. Additional methods for the identification of specific ecological or environmental hazards are needed.

b) Gene Flow

Rationale
Gene flow from LM mosquitoes has the potential to create new pests by the transfer of the modified traits to wild populations and to non-related organisms. The possible mechanisms of gene flow are:

Vertical – Vertical gene flow is the movement of genetic information from one organism to another through sexual transmission. The potential of this happening depends on the trait conferred upon the recipient insect, whether it can become more fit.

Horizontal - Horizontal gene flow is the movement of genetic information from one organism to another through means other than sexual transmission and could occur between completely unrelated organisms. This will depend upon the kind of gene drive mechanism used to develop the LM mosquitoes. Risks may be difficult to quantify without specific information on frequencies and mechanisms on such exchanges.

The roadmap is meant to provide a reasoned guidance on how to apply in practice the necessary steps for environmental risk assessment as laid down in Annex III of the Protocol. The roadmap also shows how these steps are interlinked.

Whether gene flow occurs and what undesirable effects it might have depends on various factors, such as the LM technology used, the trait or traits carried by the LM insects, etc. For many of the approaches for reducing vector competence, a gene drive mechanism giving high rates of intraspecific gene flow into wild populations is a desired trait.

Topics to consider:

- Does the release of the LM mosquitoes have the potential to create new pests, pass their modified traits to wild populations and to non-related organisms? If so, what are the undesirable consequences?
- Will the LM mosquitoes induce undesirable functions or behaviors within target species, other wild related species, or non-related organisms?

c) Ecologically mediated effects to human health

Rationale

It could happen that the released LM mosquitoes do not behave as expected. Gene silencing or other production failures may result in the release of non-sterile or competent mosquitoes and thus increasing the vector population or pathogen transmission. Suppression of target mosquito could allow a different vector species to become more widely established, resulting in increased risk of human morbidity or mortality. LM mosquitoes could transmit a different disease, such as dengue and chikungunya, more efficiently, resulting in human morbidity or mortality.

Topics to consider:

- Quality control of the released population
- Monitoring strategies

d) Evolutionary responses (especially in vector or pathogen)

Rationale

Evolution is a continuous process, depending on severla factors, but inevitably leading to resistance against effects that decrease the organisms's fitness. Mosquito vector might evolve to avoid population suppression, regain vector competency, or acquire new or enhanced competency of another disease agent. The disease agent might evolve to overcome the limitation posed by the genetic modification, and thus could become more virulent, overcome non-competency mechanism, or acquire new vector species.

Topics to consider:

- Risk management options
- Development of simple monitoring methods

e) Persistence of the transgene in the environment

Rationale

Inserted transgene(s) may spread and persist in the natural population. Some LMM transgenes are designed not to persist and others are expected to spread rapidly in the wild population. If the LMM causes unexpected and unacceptable adverse effects on human health, methods to reduce the persistence of the transgene in the environment or to mitigate the expression of the transgene may be needed.

Topics to consider:

- Risk management options
- Monitoring strategies

OTHER ISSUES

There other dimensions that should be taken into consideration in the decision for environmental releases of LMMs which are not governed by Anex III of the Cartagena Protocol. These dimensions encompass among others, economic, health and social trade-offs associated with the technology application, as well as social and cultural issues expected to influence acceptance of these methods.

RISK MANAGEMENT OPTIONS

Risk assessors might want to consider the following risk management strategies for the release into the environment of LMM:

- Monitoring for transgene intactness and proper function over time.
- Monitoring during and after the environmental release of LMM to address species replacement before it becomes an irreversible problem;
- Halting the releases if unanticipated effects occur; halting the releases will allow the pre-release state to naturally return;
- Stringent controls on release mechanisms / strategies
- Genetic controls
- Mitigations, such as an alternative control set of measures should a problem occur.

BIBLIOGRAPHY