# C. RIsk Assessment of Living modified mosquitoes

# Introduction

Living modified (LM) mosquitoes are being developed through modern biotechnology to reduce transmission of vector-borne human pathogens, particularly those that cause malaria, dengue and chikungunya. Control and reduction of such diseases, is a recognized public health goal. The impacts of such diseases on human health are staggering. For instance, in 2008, there were 247 million cases of malaria and nearly one million deaths.[[1]](#footnote-1) Therefore, specific and comprehensive considerations should be undertaken with regard to the potential benefits and adverse effects of LM mosquitoes.

The biology and ecology of mosquitoes, on the one hand, and their impact on public health as vectors of human and animal diseases, on the other hand, taking into account that virtually all these have sylvatic zoonotic reservoirs, pose specific considerations and challenges during the risk assessment process.

Two strategies of modern biotechnology, namely self-limiting and self-propagating strategies, are being developed to produce LM mosquitoes to control vector-borne diseases.

Self-limiting strategies are being developed to control mosquito vectors by suppressing their population or reducing their competence by developing LM mosquitoes that are unable to produce viable offspring.

LM mosquitoes that are developed under self-limiting strategies are intended to prevent the passage of the modified trait to subsequent generations, e.g. by interrupting larval development. Modern biotechnology techniques for the development of self-limiting LM mosquitoes populations (e.g. “Release of Insects carrying a Dominant Lethal” or RIDL) are different from those based on the use of irradiation to induce male sterility since they target behavioural sterility of female populations. Other self-limiting strategies target metabolic processes of the mosquito vectors and aim at lowering their fitness and reducing their populations.

Self-propagating strategies, also known as self-sustaining, rely on *[gene-drive systems](#genedrive_system)* that promote the spread and persistence of the transgene through populations of the same mosquito species. As opposed to the self-limiting strategy, the modifications in the LM mosquitoes produced through self-propagating strategies are intended to be heritable and to spread through the target population and, thus, to persist in the ecosystem at least in the medium term. The objective of the self-propagating strategies is, hence, population replacement of the non-modified mosquitoes by the LM mosquitoes.

Another strategy, the so-called paratransgenesis, is under development to control, reduce or eliminate the capacity of the mosquitoes to transmit pathogens mainly, but not exclusively, by blocking the development of the pathogen in the vector. Paratransgenesis focuses on utilizing LM symbionts of insects to express molecules within the vector that are deleterious to the pathogens they transmit. So rather than genetically modifying the mosquitoes, the focus of paratransgenesis is on the genetic modification of microorganisms that inhabit the mosquito midgut. Such microorganisms may have a specific, symbiotic relationship with the mosquito, or it may be commonly associated with the mosquito but not have an obligate relationship. Paratransgenesis can be used as a self-limiting strategy for population suppression or as a limited self-propagating strategy for population replacement (see above). It is noted that although in the case of paratransgenesis the mosquito itself will not be genetically modified, the symbionts or parasites will most likely be the product of modern biotechnology, and therefore this type of strategy is also being mentioned here.

The mosquitoes developed through the different strategies will differ, for example, in their ability to persist in the environment and to spread the inserted transgenes into the local mosquito population, or even into other organisms. Therefore, the risk assessment needs and criteria will depend on the specific characteristics of the LMO and the strategy used.

1. WHO (2010) Malaria fact sheet. Available at <http://www.who.int/mediacentre/factsheets/fs094/en/>. [↑](#footnote-ref-1)