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MosqGuide: A project to develop best practice guidance for the deployment of innovative genetic vector control strategies for malaria and dengue

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Abstract. The World Health Organisation Special Programme in Research and Training in Tropical Diseases (WHO/TDR) has funded a project, designated MosqGuide, to develop guidance on the potential deployment of different types of genetically modified (GM) mosquitoes to control vector borne diseases, specifically malaria and dengue. This guidance is intended to support disease endemic countries (DECs) and other stakeholders in considering the safety and legal/regulatory aspects, as well as ethical, cultural and social issues, of such deployment. Commissioned in 2008 as a three year project, MosqGuide will result in a series of best practice documents developed by the project's international team of experts in regulation, vector control and management, arthropod molecular biology, social sciences and environmental risk assessment. Using fundamental principles of risk/benefit as a foundation, the MosqGuide project will prepare guidance as a series of modules aimed at different user groups, including researchers, regulators, public health officials, funding bodies and interested public. Each module will be tested with target audiences, primarily regulators and decision makers in the DECs, and will also feed into other WHO initiatives, such as the Regional Biosafety Training Centres for GM Vectors. The guidance will also include a module that demonstrates a prototype issues/response model to assist DECs in making an informed choice about whether and under what conditions to deploy specific genetic control methods for the control of mosquito vectors for malaria and dengue.

Keywords: Malaria, Dengue, Guidance, Risk Analysis, Mosquitoes, Regulation, Safety, Genetic Modification

The prospect of genetic control methods (Alphey *et al.*, 2002; Scott *et al.*, 2002) against mosquito vectored human diseases is rapidly approaching a reality. There have been significant advances in this field and within the next 2-5 years efficacy testing of genetically modified (GM) mosquitoes engineered for population suppression traits may take place in field cages and the open environment (e.g. Malaysia, Mexico, Panama, Brazil and India). With the potential of a promising additional method for dengue and/or malaria disease control on the horizon, many decisions will need to be made on a national, regional and international level regarding the biosafety, social, cultural and ethical aspects of the use and deployment of these vector control methods (Takken *et al.*, 2002; Knols *et al.*, 2004; Lavery *et al.*, 2008). Their relevance, effectiveness and efficiency must be judged against diverse criteria across these various dimensions and they must also stand up to comparisons with alternative, conventional measures for vector and disease management, or prove worthy as a new intervention to add to an integrated control programme.

The MosqGuide project, led by the Centre for Environmental Policy at Imperial College London, has created a network of expertise in vector biology, genetics, disease control, regulation, social science and risk analysis from the UK, Panama, Brazil, Mexico, Thailand, Kenya and India. The purpose of the network, which is funded by the WHO Special Program for Research and Training in Tropical Diseases (TDR) is to prepare guidance on best practices, peer reviewed literature, emerging data and related experiences of risk assessment and management. The project itself is not involved in any field release programmes, although partners may be under separate funding. The project was launched in July 2008 with a network meeting at Imperial College London where the parameters of the guidance were specified. The MosqGuide project will address issues

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surrounding the deployment of GM vectors where the mosquito deoxyribonucleic acid (DNA) has been directly modified, but it will not include other potential strategies to control mosquito vectors, such as paratransgenesis (Riehle *et al*., 2007). The guidance will also concentrate efforts on addressing technologies likely to reach field use within ten years of the project start date (for implementation up to 2018).

The guidance is being prepared as seven modules, each with a specific target audience. Module 1 will present an overview for all audiences and consists of documents describing the objectives and parameters of the project, how to use the materials produced, technology options, and the bio-ethical, social and regulatory issues that have been raised in relation to these. Some of these have already been created and can be found on the project website (www.mosqguide.org.uk). The regulatory component, linked also with Module 3, will present internationally accepted risk analysis principles as the foundation for decision making, with risk ranking criteria. MosqGuide will initially focus on lower risk options such as genetically induced sterility, which can be employed in a similar way to current radiation-induced sterile insect release, which is widely used for controlling Tephritid fruit flies in the US, Argentina, Spain and other countries. GM vector options with a higher perceived risk, such as gene drive strategies, to produce transmission inhibited populations, or self sustaining constructs will be addressed later. This would seek to complement the guidance prepared on cage trials through the Bill and Melinda Gates Foundation/Foundation for the National Institutes of Health (FNIH) consortium, which described measures for testing under highest risk scenarios (Benedict *et al*, 2008; Knols *et al*., 2004).

Module 2 brings together best practice and experiences with the technology research and production phase, and is directed to researchers in the field. Further insight has been obtained by the use of a questionnaire at international meetings to determine current practice in the laboratory with genetically engineered insects. Mass rearing of insects will form a separate component of this Module as there is much to be learnt from the existing mass rearing programmes from the sterile insect technique (SIT). Consideration of costs will come under Module 3, based on some of the findings in Module 2. To further this MosqGuide personnel are consulting with the International Atomic Energy Agency (IAEA) and working from similar costing information for other mass reared insects (Quinlan *et al*., 2008).

Module 3 focuses on internal national decisions, including clarification of objectives and internal site selection. It will describe model national regulatory processes, such as processes for permitting field trials, using examples of other intentional insect release activities and the few existing cases of GM vectors. Module 3 has started in year 2 of the project, along with Module 4 on field data collection and monitoring. Module 5 is a case study on national decision making, including public consultation, regarding the use of GM vectors as an additional method for *Aedes aegypti* control to reduce dengue in countries currently undergoing that process. It is anticipated that examples will include Malaysia, Brazil and Panama.

Module 6 is ongoing and would link the project to external training through co-ordination with the TDR funded Regional Biosafety Training Centres in Mali, India, and Colombia. Courses have already been held at Bamako, Mali, Medellín, Colombia and Madurai, India in 2008/9, with inputs from MosqGuide partners. The close involvement of MosqGuide with the Biosafety Training Centres is helping to ensure that materials produced by the project have practical applicability in training curricula. Interaction with participants in the courses, who are most directly involved in the implementation of potential GM vector control technologies, is an important part of the validation process for guidance. The project will aim to provide course curricula relevant to GM technologies for the training courses, as well as to continue to attend regional courses to maintain the valuable dialogue with workers in the field. Leaders from the Regional Biosafety Training Centres have been invited to participate in MosqGuide planning meetings and workshops.

The project culminates in Module 7, which will provide a prototype decision support tool that will use biological and ecological data along with socio-economic conditions to demonstrate case-specific advice on regulatory and implementation decisions. As this is not an advocacy project, but rather an attempt to lay out best practice, a decision to not deploy GM vectors is as valid an outcome as to deploy them, after due consideration. Work has begun on choosing the parameters to include in this prototype model. Module 7 will be in development throughout the remainder of project period.

Over the coming years the plan is that relevant components of Modules are validated through cooperation with collaborating European Commission funded projects conducting laboratory work with GM vectors in Africa and Europe, as well as with other projects in Asia. Wide consultation in the project is envisaged to collect, validate and communicate best practices, and to assist with the development and testing of the MosqGuide modules as they develop. MosqGuide also brings together laboratory based researchers with field experts for dialogue and discussions and this will continue for the future of the project. MosqGuide welcomes comments on the modules in development and these will be posted on the website when they are available.

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