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Ethical, legal and social issues in the use of genetically modified vectors for disease control

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Abstract

Genetic control of vectors may have an important role to play in the interruption of vector-borne disease transmission if the main biotechnological and implementation challenges are adequately addressed. Following the demonstration, in the laboratory, of the technical feasibility to develop transgenic mosquitoes unable to transmit malaria and dengue pathogens, the following actions will need to be taken in order to make this approach a control method applicable for public-health purposes: establish a proof of efficacy and safety to be approved by authorized biosafety and regulatory bodies before any experimental release; ensure the public and the media that this goal is desirable, feasible and can be accomplished safely; develop a plan to gather all the information necessary for legal and regulatory approvals; design a monitoring system for early detection and evaluation of adverse outcomes and plan strategies to remedy their effects; develop mechanisms for dissemination of information; enhance capacity in disease-endemic countries, promote research partnership and create an international consortium for genetic control of disease vectors to coordinate research activities and suggest future directions.
Keywords: vector-borne diseases; genetic control; efficacy; Biosafety assessment; Ethical, legal, social issues; Interruption of transmission

Current state of the art

The technical feasibility of the development of transgenic mosquitoes unable to transmit malaria and dengue pathogens has been demonstrated in the laboratory. *Anopheles stephensi* was made refractory to *Plasmodium berghei* growth and transmission (Ito et al. 2002) and *Aedes aegypti* was made resistant to DEN-2 virus replication and transmission (Olson et al. 1996). However, key issues remain to be addressed in order to make this approach a control method applicable for public-health purposes. They include biotechnological challenges dealing with the development of the tool, such as devising suitable gene driver systems and developing and evaluating appropriate effector gene constructs. They also consist of implementation challenges for the use of the tool in the field. The requirements to be considered before genetic control methods, in general, can be used in the field and refractory transgenic insect vectors, in particular, can be released into the wild, comprise the need to demonstrate a proof of efficacy and safety for humans and the

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environment, and to address Ethical, Legal and Social Issues (ELSI) (Alphey et al. 2002; Macer 2003). These matters represent important considerations to address in order to ensure the public about the efficacy and safety of the control strategy and develop an evidence base for policy decision-taking. Consequently, lessons are to be learned from the genetically modified food debate and previous experiments about genetic control of vectors in El Salvador and India (see Curtis, this volume, Chapter 3).

Issues and challenges

The main issues to consider include:

- *To provide a proof of efficacy and safety of the use of genetically modified vectors (GMVs) for disease control*

  Laboratory experiments and contained semi-field tests would need to be undertaken under different conditions and during a sufficient period of time to provide the evidence that the tool is efficacious and safe.

- *Biosafety assessment and management to minimize potential risks for humans and the environment*

  Proper safety assessment and management is an important basis for policy decision. It needs a strong scientific base such as the identification of scientific principles and practices for conducting safe laboratory experiments and field trials with GMVs, following Good Developmental Practices (GDP) (Touré et al. 2003; Touré, Oduola and Morel 2004). It also requires the setting up of procedures during the research and development process to minimize the potential adverse human and environmental consequences by anticipating detrimental effects that might follow the release of GMVs during experimentation. In addition, it can be achieved through the provision of guidance on the design and performance of minimum-risk field research, the development of criteria and test methods for environmental monitoring, the provision of the basis for collection of data addressing safety in the field and, finally, the development of guidelines for dispersal, contingency measures and site rehabilitation (Macer 2003). Moreover, it would need the design of monitoring systems for early detection and evaluation of adverse outcomes, and of the planning of interventions strategies, so that new information can be gathered and interpreted to avert and, if necessary, remedy adverse health or environmental effects (Edmonds Institute 1998).

- *Site selection and preparation*

  There should be prior environmental and health studies for site selection, and based on these data the most appropriate sites should be chosen. In this regard, ecological studies are needed to improve understanding of gene flow in vector populations (mating patterns, behaviour, male biology, population size and structure, mechanisms of population regulation, fitness and phenotypic effects of colonization and mass production). They will help identifying suitable isolated field sites, characterize vector populations in terms of genetic and ecological make-up, determine epidemiological patterns (transmission, disease), and develop appropriate contained semi-field systems to improve understanding of the biology of (transgenic) vectors (Scott et al. 2002). Furthermore, models can be used to enhance understanding of biological processes, spatial and temporal variations, selection of ‘suitable’ areas, prediction of effects of transgene introduction and public-health outcome.

A proof of efficacy and safety to be approved by authorized biosafety and regulatory bodies before any experimental release should be properly established (Hoy 2000; Macer 2003).

- *To address the Ethical, Legal and Social Issues (ELSI) of the potential use of GMVs*

ELSI of the potential use of GMVs need to be properly addressed through the following actions:

– Integrating with the scientific studies those ELSI factors that are relevant to the use of GMVs and ensuring that the biosafety information reaches the public, the communities and the decision-making bodies.

– Ensuring that all stakeholders (i.e. parties with legitimate concerns) have mechanisms for including their input into the proposed control programmes.

– Translating risk assessment procedures into language(s) that is (are) easily understood by the communities concerned.

– Collaborating with end-users on rationale and practical bases for the choice of sites and planning for deployment, in clear and legally appropriate concepts of informed consent. Consent should be obtained from the communities involved. The mechanisms to obtain individual and group consent need to be specifically developed for public-health interventions.

– The data should be openly provided to all as broadly as possible in a two-way process, so that they can benefit from global expertise and develop an international consensus.

– Building public awareness and confidence about the benefits and risks in order to develop implementation strategies that involve the end-user communities and decision-making bodies and to provide means to the public (including the media) to be sufficiently knowledgeable to understand the real measures of success of the programmes and to make informed decisions about the merits of deploying these programmes in their communities.

– Provide adequate means for information dissemination and communication.

– Promote South-South and South-North research cooperation, develop partnerships and enhance capacity in disease-endemic countries (DECs) for the understanding and the potential use of the control tool.

- *Gather all the information necessary for legal and regulatory approvals*

The efficacy and biosafety data gathered along with the actions taken with the public, the media and the communities will be used to provide a complete documentation for biosafety review, ethical review and approval by national and local authorities. A global endorsement (international level) would be most desirable to allow multi-country implementation of the strategy.

Research and control opportunities

Despite the international commitment to control vector-borne diseases such as malaria and dengue, the disease burden still remains high. Under such circumstances, the ultimate goal for vector-borne disease control remains the interruption of transmission. Genetic control of vectors would have an important role to play in the interruption of transmission if the challenges indicated above are adequately addressed.

The ongoing research activities with support from WHO/TDR, NIAID/NIH, IAEA, Wageningen University and the forthcoming Gates Foundation-supported activities

provide a basis for concerted efforts to address the challenges. A coordination of the research activities and the organization of a network would strongly enhance our ability to address the challenges. The creation of a consortium to coordinate the network activities from the different sources of support would be needed. The activities of the consortium may involve an annual meeting to review the progress achieved and suggest future direction.

Future directions for research and capacity/partnership building

The main goal would be to undertake the actions necessary to provide proof of efficacy and safety and address public concerns as bases for policy decision. The actions would include:

- *To provide a proof of efficacy and safety of the use of GMVs for disease control*

– Conduct studies on efficacy, biosafety and risk/benefit evaluation through long-term efforts to clarify the scientific uncertainties under different experimental conditions and with the involvement of investigators in DECs.

– Provide the basis for collection of data on vector biology, ecology, behaviour and genetics addressing efficacy and safety in the field.

– Develop guidelines and principles on the design and performance of efficacy and minimum-risk field research.

– Develop criteria and test methods for environmental monitoring.

– Develop criteria to identify and prepare the sites.

– Design monitoring systems for early detection and evaluation of adverse outcomes, and plan interventions strategies, so that new information can be gathered and interpreted to avert and, if necessary, remedy adverse health or environmental effects.

– Develop guidelines for dispersal, contingency measures and site rehabilitation.

- *To ensure the public that this goal is desirable, feasible and can be accomplished safely*

– Develop a strategy to make the information available to the public and the media such as to raise their awareness and address their concerns about possible environmental and human-health risks.

– Bring all parties together on common ground that can lead to objective, scientific, legal, ethical and social-based decisions by policymakers bearing in mind that most people may not trust the scientific risk analyses.

- *To develop a plan to gather all the information necessary for legal and regulatory approvals*

– Documentation for biosafety review.

– Documentation for ethical review.

– Documentation and mechanisms for national and local authorities' approval and international endorsement.

- *To enhance capacity in DECs* for biosafety assessment, risk/benefit evaluation, environmental monitoring, and research on vector biology, ecology, genetics and behaviour.
- *To promote South-South and North-South research collaboration* based on well defined ethical and scientific standards.
- *To develop mechanisms for dissemination of information* to researchers, decision makers, the communities, the public and the media.
- *To create an international consortium for genetic control of disease vectors* to coordinate the research activities and suggest future directions.

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