Regulatory & Policy Approaches to the Diversity of Gene Drives

Owain Edwards | 19 May 2022
Risk Associated with the Release of Wolbachia-Infected Aedes aegypti Mosquitoes into the Environment in an Effort to Control Dengue

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Learnings from Wolbachia regulatory assessment

1. Use existing generic risk assessment frameworks

2. Take advice from all available relevant guidelines

3. Engage with all stakeholder groups (Experts -> General Public) to identify gaps
A phased testing pathway is recommended, in which new GMM strategies move from the laboratory, to testing in more natural environments under confined conditions, and finally to open release trials, with each transition dependent upon satisfactory demonstration of efficacy and safety.
Fig. 1.3. Phased testing pathway for GMMs

Phase 1: Laboratory Studies → Population Cage Studies → Physically Confined Field Studies → Staged Open Field Releases → Post-Implementation Surveillance

Phase 2: Ecologically Confined Field Studies

Fig. 1.4 Modified testing pathway for GMMs with low-threshold drive systems

Phase 1: Laboratory Studies → Population Cage Studies → Physically Confined Field Studies → Small-scale Isolated Releases → Small-scale Open Releases → Large-scale Open Releases → Post-Implementation Surveillance
Ecological/Genetic containment

Technological steps:
1. Non-driving form
2. Drive without cargo/disruption
3. Split drive approaches
4. Genetic localization technologies

Validation of modelling
Pest risk analysis for quarantine pests
1. Probability of Introduction (species or genotype/phenotype)

2. Probability of Establishment (and Spread)

3. Potential Economic/Environmental Consequences

4. Pest Risk Management
ANNEX 2:
Pest risk analysis for living modified organisms (LMOs)
Pest Risk Analyses of LMOs

- Useful to consider risks relative to unmodified organism
- **Direct effects**: altered pest characteristics
- **Indirect effects**: quality/prevalence of other species due to effects of modification
Systematic identification of plausible pathways to potential harm via problem formulation for investigational releases of a population suppression gene drive to control the human malaria vector \textit{Anopheles gambiae} in West Africa

John B. Connolly, John D. Murfard, Silke Fuchs, Geoff Turner, Carrilla Beech, Ace R. North and Austin Burt.
ADDITIONAL STEPS FOR GENE DRIVE ORGANISMS?

• Probability of spread after establishment into other regulatory jurisdictions
Fig. 1.4 Modified testing pathway for GMMs with low-threshold drive systems²
MODELLING MOVEMENT of INVASIVE SPECIES

1. Natural (wind-borne) movement
2. Human-assisted movement
TAPPAS (Tool for Assessing Pest & Pathogen Aerial Spread)
ASIAN-PACIFIC SHIPPING LANES

Schmidt et al. (2020)
GENOMIC ASSESSMENTS OF FRUIT FLY INCURSIONS

2014, 8 Qfly breeding in suburban Auckland
GENOMIC ASSESSMENTS OF FRUIT FLY INCURSIONS

2018, 2 Qfly established in Auckland suburb
TAKE HOME MESSAGES

1. To cover the diversity of gene drives, use an established, generic, case by case regulatory assessment approach

2. Take advice from published guidelines and by engaging all relevant stakeholders

3. Field releases should be staged not just by scale (small -> large) but also by technology (non-drive, drive with no cargo, split drive, etc.)

4. Likelihood of spread between jurisdictions after establishment should be examined in depth for gene drive organisms