Policy and Regulatory Issues for Gene Drives in Insects: *Results of a Workshop*

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What is a Gene Drive?

- Initially coined to describe the process of stimulating biased inheritance of particular genes to alter entire populations
- Now increasingly used to describe the synthetic genetic element itself
- “Non-Mendelian” inheritance

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Examples Under Development

- Modified mosquitoes to control malaria:
  - 500 million cases, 0.5 million deaths per year
  - *Anopheles stephensi* (prevent transmission)
  - *Anopheles gambiae* (population suppression)
- Modified insects to control agricultural pests:
  - Spotted Wing Fly (pest of soft fruits)
  - Citrus Greening Disease
  - Diamondback moth (GE but not gene drive)

Results of a Two Day Workshop January 2016

- Participants:
  - Scientists working to develop insects with gene drives
  - Technology funders
  - Federal regulators, State Dept., international orgs.
  - Ethicists, ecologists, and environmental policy analysts
  - Experts in laboratory biosafety and insectary standards
  - Scientists with experience conducting field trials of GE insects and traditional biocontrol organisms
- Funders:
  - Legler Benbough Foundation
  - UC San Diego, Office of Chancellor
  - JCVI

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Workshop Goals

- Identify a path to successful application of a gene drive insect (recognizing that may not be possible)
- At each step in phased pathway, explored
  - Experience to date
  - Regulatory and risk assessment information needs
  - Other gaps in knowledge
  - Challenges in earning public trust

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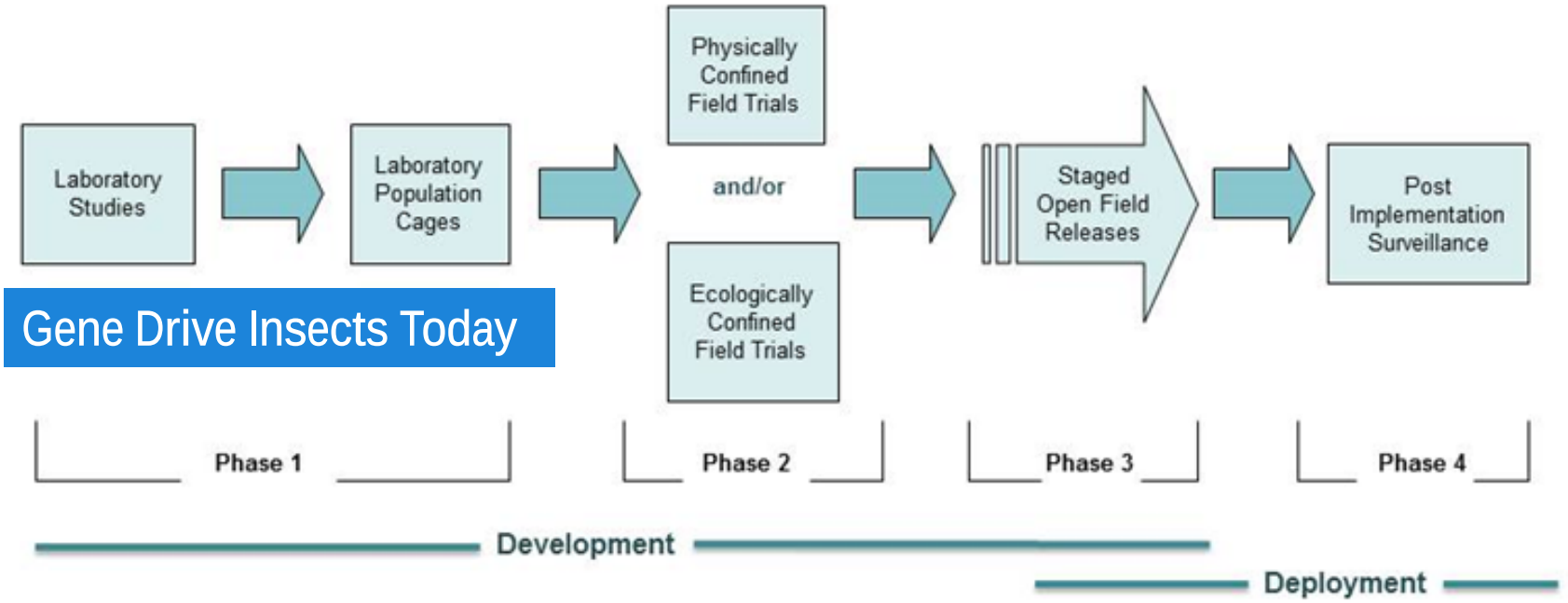
Phased Testing Pathway for Genetically Modified Mosquitos



credit: WHO-TDR and FNIH, 2014.

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Suggestions

- “Action Items” identified for each of three key groups of actors:
  - Researchers and research funders
  - U.S. regulators and policy makers
  - International organizations

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Suggestions to Researchers and Research Funders

Support Research to Develop New and Varied Gene Drive Technologies

Table 1 | **Comparison of the various types of gene drive systems**

	Homing-based drive	X-Shredder	*Medea*	Toxin–antidote underdominance	Chromosomal rearrangement	*Wolbachia*
Type	Either	Suppression	Replacement	Replacement	Replacement*	Replacement‡
Rate of spread	Fast	Moderate	Moderate	Slow	Slow	Moderate
Locally confined?	No	No	No, if low fitness cost§	Yes	Yes	No, if low fitness cost§
Resistance allele generation rate	High	Low	Low	Moderate	Very Low	Unknown
Reversible?	Yes	Yes	Yes	Yes	Yes	No
Removable with wild type?	No‖	No‖	No, if low fitness cost§	Yes	Yes	No, if low fitness cost§
Status	*Drosophila*[17], *Saccharomyces*[16], *Anopheles stephensi*[21], *Anopheles gambiae*[22]	Incomplete in *Anopheles gambiae*[76]	*Drosophila*[19,20]	*Drosophila*[18,96]	Natural examples[89,94]	Field tests[111,112]

The characteristics listed here are variable and depend on a range of factors (for example, ecology of the target species, population distribution, movement patterns, fitness costs, payload characteristics, and so on); therefore, only ideal-case scenarios are compared to emphasize intrinsic differences of the various types of drives. *Chromosomal rearrangement can be used for short-term population suppression. ‡It is possible that male-killing strains of *Wolbachia* may be usable for population suppression. §High fitness costs may make these systems locally confined and removable with the release of large numbers of wild-type organisms. ‖Suppression types that proceed to fixation and eliminate a population will remove the gene drive system, allowing replacement with wild-type organisms.

from Champer, Buchman, Akbari, 2016

Suggestions to Researchers and Research Funders (cont.)

Regarding Gene Drive Technology Development and Products That Might Use Them:

- Support research to develop new gene drive technologies with varied characteristics
- Design applications to meet multiple objectives using the full range of available (and to be developed) gene drive technologies

Suggestions to Researchers and Research Funders (cont.)

Community Engagement

- Incorporate community engagement activities as a critical component of field testing and deployment
  - Perhaps the strongest consensus to emerge during the workshop

Suggestions to Researchers and Research Funders (cont.)

Guidance Documents on Best Practices

- Review and update existing non-governmental guidance documents.
  - Needed for all 4 phases
    - American Society of Tropical Medicine and Hygiene
    - Policy Forum in Science magazine
    - Gates/FNIH guidance on contained field trials
- Develop guidance for community engagement

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Suggestions for U.S. regulators and policy makers

Suggestions for the Office of Science and Technology Policy

- Establish a “single door” approach to the biotechnology regulatory system.
- Clarify the roles of the regulatory agencies

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Suggestions for U.S. regulators and policy makers (cont.)

Suggestion for NIH

- Within NIH Guidelines, develop additional guidance for lab experiments using gene drives

Suggestion for FDA

- Clarify how FDA regulatory process might incorporate a staged-release approach, including environmental assessments

Suggestions for U.S. regulators and policy makers (cont.)

Suggestions for USDA/APHIS

- Develop a framework for staged field testing and deployment of gene drive insects.
- Evaluate and, if necessary, update laboratory containment guidelines.

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Suggestions for international organizations

Suggestions related to the World Health Organization

- Review and update existing WHO guidance and training documents
  - (WHO Special Programme for Research and Training in Tropical Diseases)
- Continue and expand review of GE mosquitoes by VCAG
  - (Vector Control Advisory Group on New Tools)

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Suggestions for international organizations (cont.)

Suggestions related to the Cartagena Protocol

- Rely on WHO to develop detailed guidance on risk assessment of GE mosquitoes
- Encourage use of bilateral and regional agreements for field trials
- Encourage others to assist regulatory capacity building for interested developing countries

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