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Problem formulation for the environmental risk assessment of gene drive modified *Drosophila suzukii*

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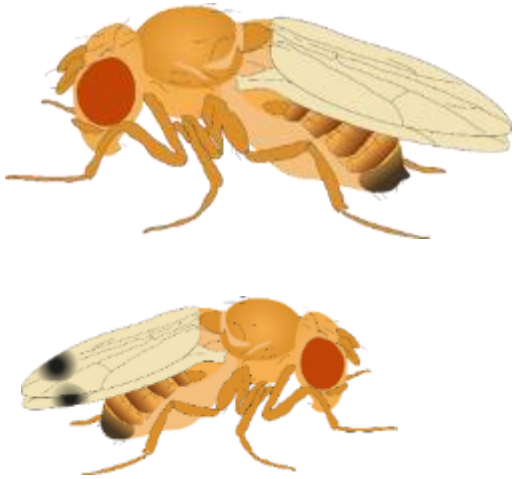

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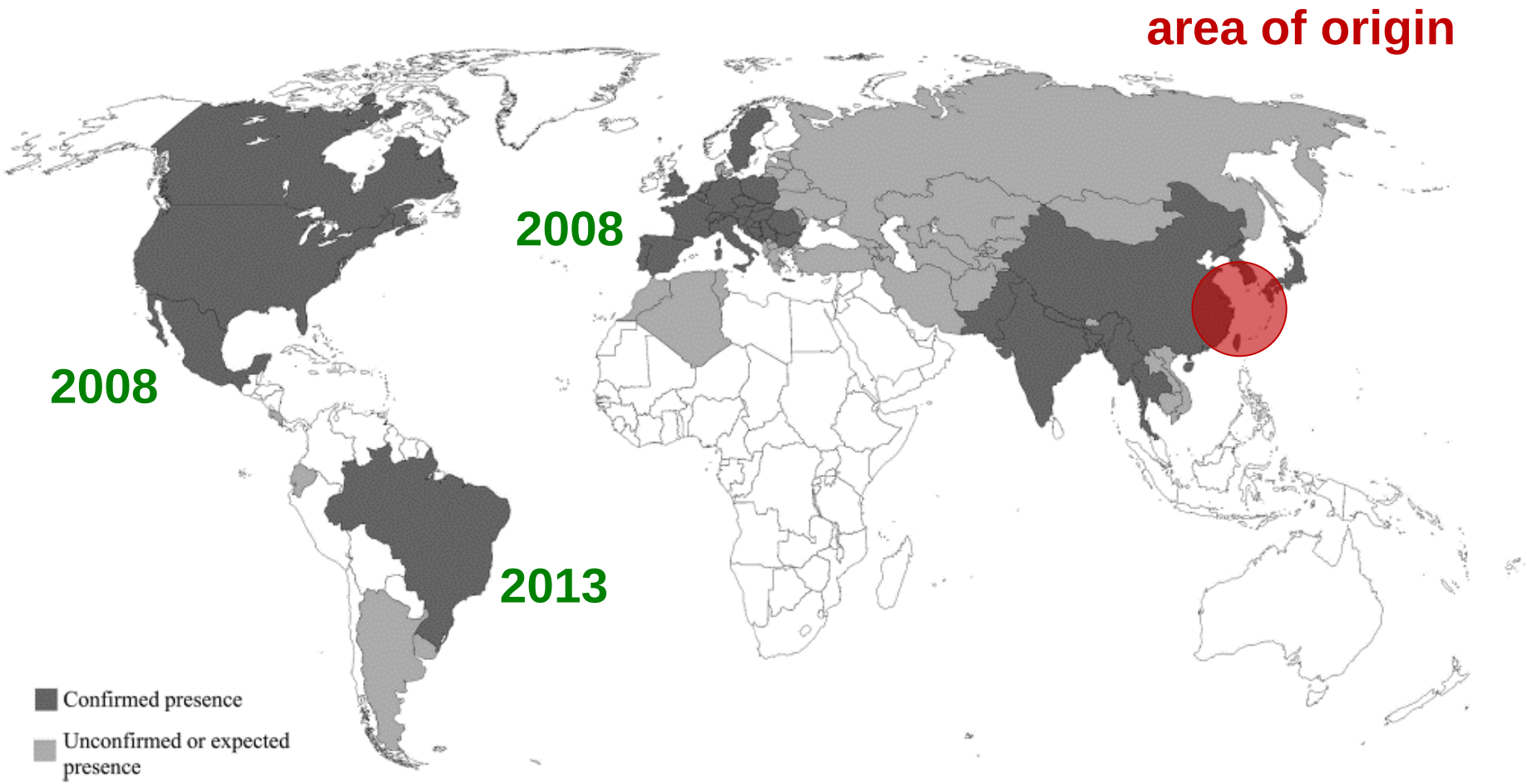
Drosophila suzukii

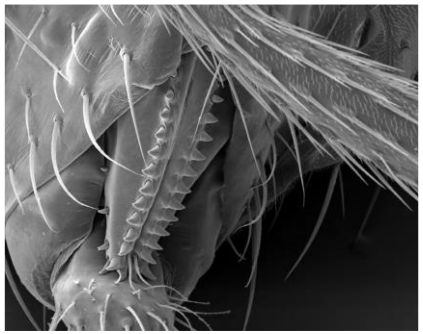
Global distribution (May 2015)

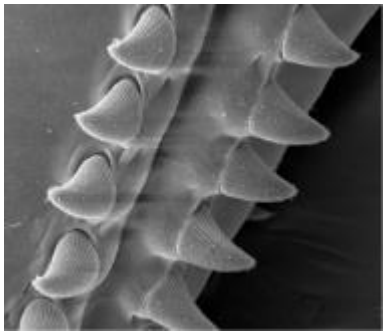


Asplen et al. 2015, Journal of Pest Science 88, 469-494

Drosophila suzukii

- Spotted wing Drosophila
- Serrated ovipositor
- Able to infest ripening, undamaged fruits
- Oviposits in stone fruit, berries, grapes, wild fruit





Pictures: Stefan Kuske; Christopher Jackson (Ikelos)

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Drosophila – ecosystem functions

- The genus *Drosophila* (Diptera: Drosophilidae) contains about 2’000 known species
- They fulfill different functions
  - Herbivory: *D. suzukii, D. subpulchrella*
  - Decomposition: *D. melanogaster, D. suboscura*
  - Pollination: *D. hydei, D. repleta*
  - Predation

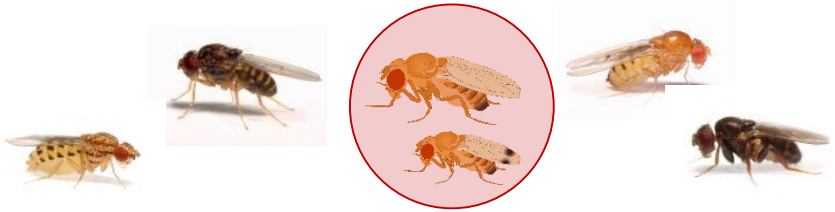
O’Grady & DaSalle 2018, Genetics 209, 1-25; Markow & O’Grady 2008, Functional Ecology 22, 747-759; Skevington & Dang 2002, Biodiversity 3, 3-27; Karremans et al. 2015, Annals of Botany 116, 437-455

Drosophila – ecosystem functions

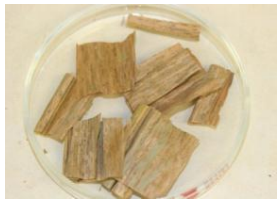
- Important food-web component

Predators

Parasitoids



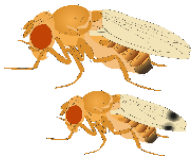
Drosophila species



Crop/ non-crop plants, senescent plant material

Gabarra et al. 2015; Miller et al. 2015; Rossi-Stacconi et al. 2015; Daane et al. 2016; Guerrieri et al. 2016; Mazzetto et al. 2016; Knoll et al. 2017; Woltz & Lee 2017; Girod et al. 2018a,b; Wolf et al. 2018; Schmidt et al. 2019

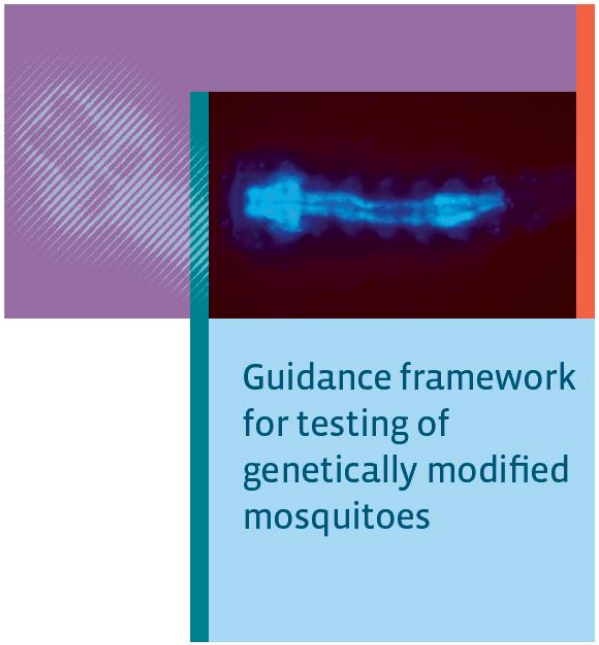
Gene drives in *D. suzukii*



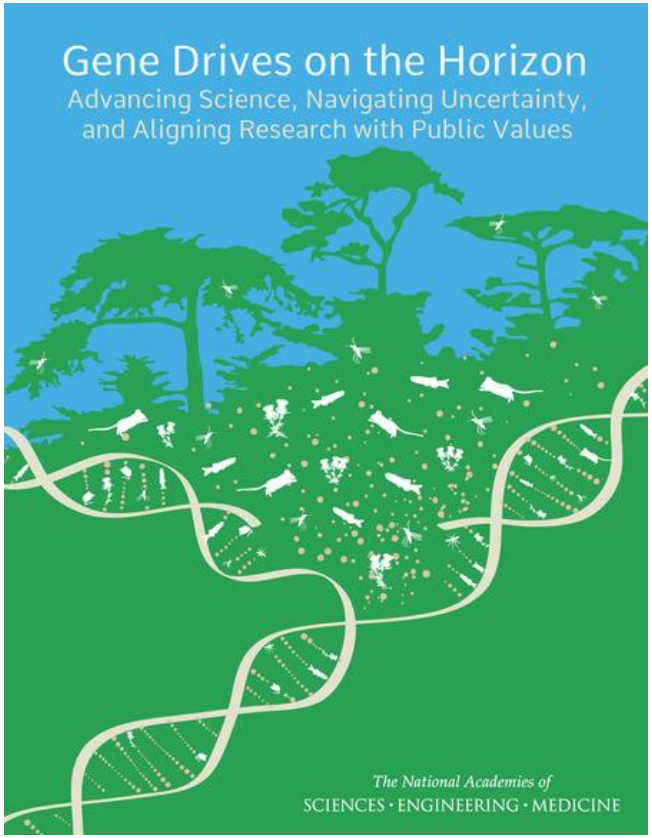
Case study

***Drosophila suzukii* with a suppression drive to be released in invaded areas**

Development of a GD organism

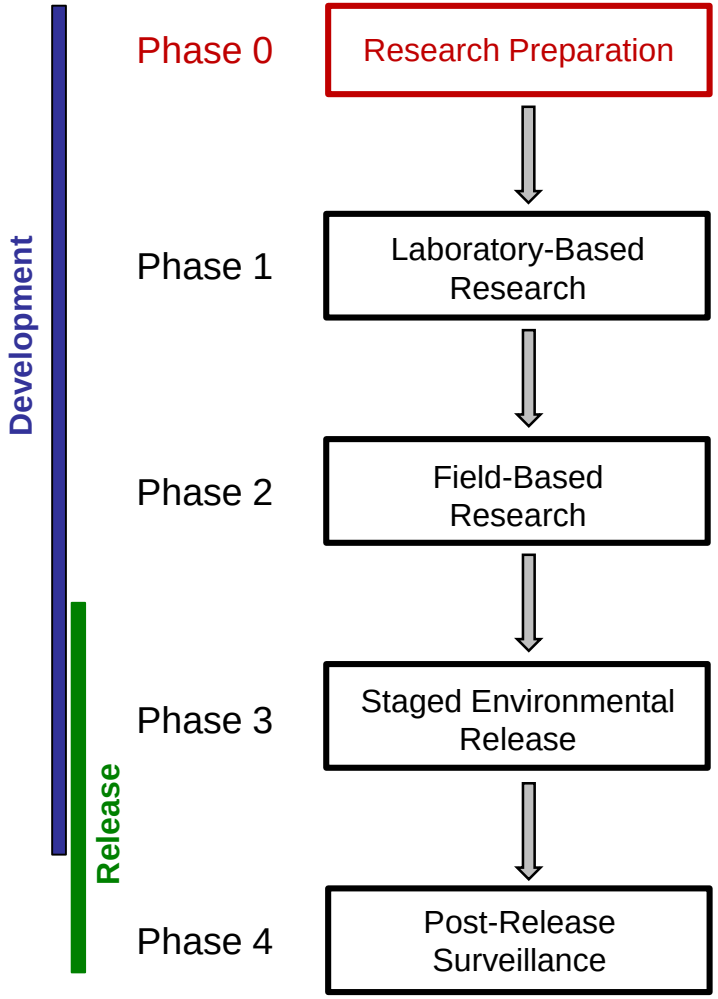


Phased testing pathway (WHO 2014)



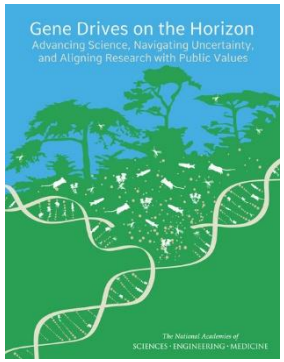
Adopted and expanded (NASEM 2016)

Development of a GD organism

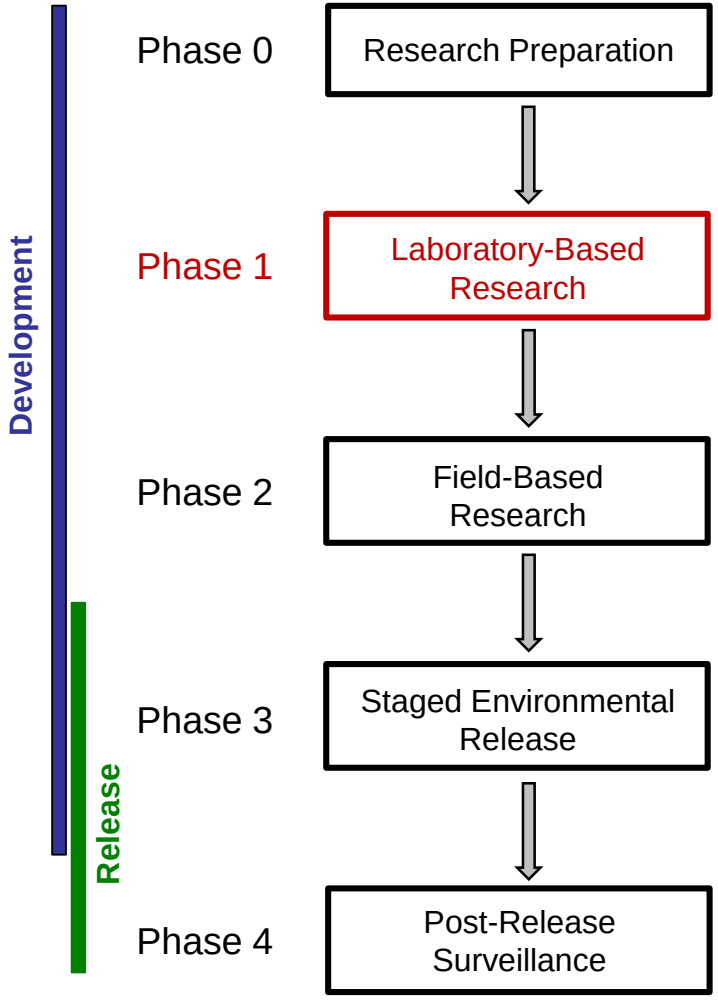


Phase 0.
Research preparation

- Target product profile
- Confinement/ containement strategies
- Develop mitigation strategies
- Engagement with policy makers

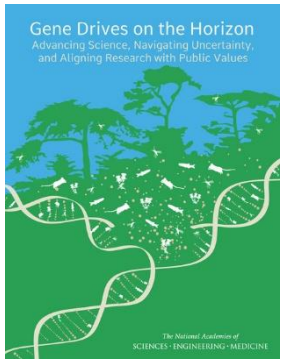


Development of a GD organism

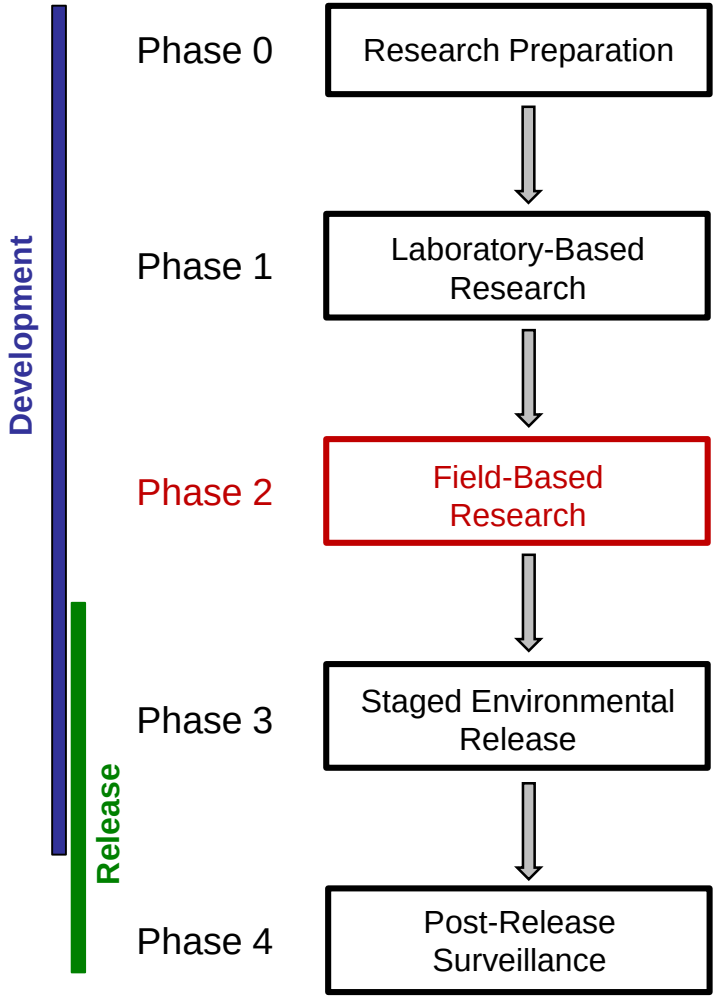


Phase 1.
Lab-based research

- Optimize drive system
  - Efficacy
  - Stability
  - Off-target effects
- Fitness/ competitiveness
- Marking of drive organisms
- Study bioconfinement and strategies to mitigate harm by unintended releases



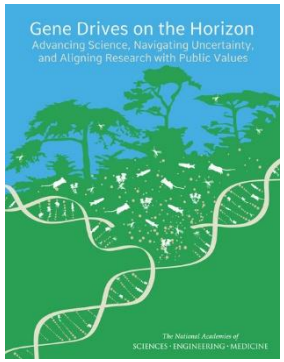
Development of a GD organism



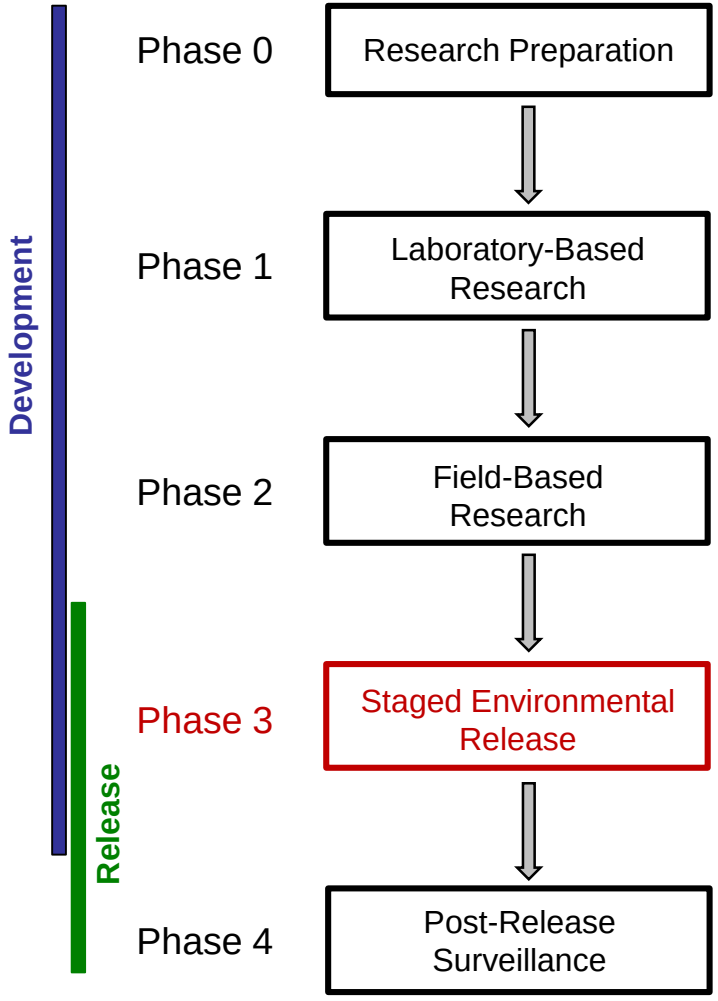
Phase 2.

Field-based research, restricted dispersal/ persistence (e.g., cages, islands)

- Validate efficacy
- Population-level effects
- Fitness/ competitiveness
- Impact on non-targets

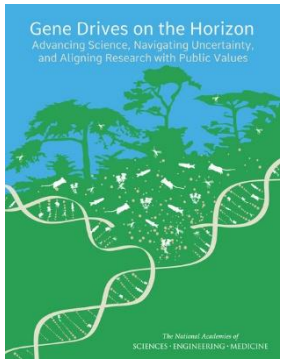


Development of a GD organism

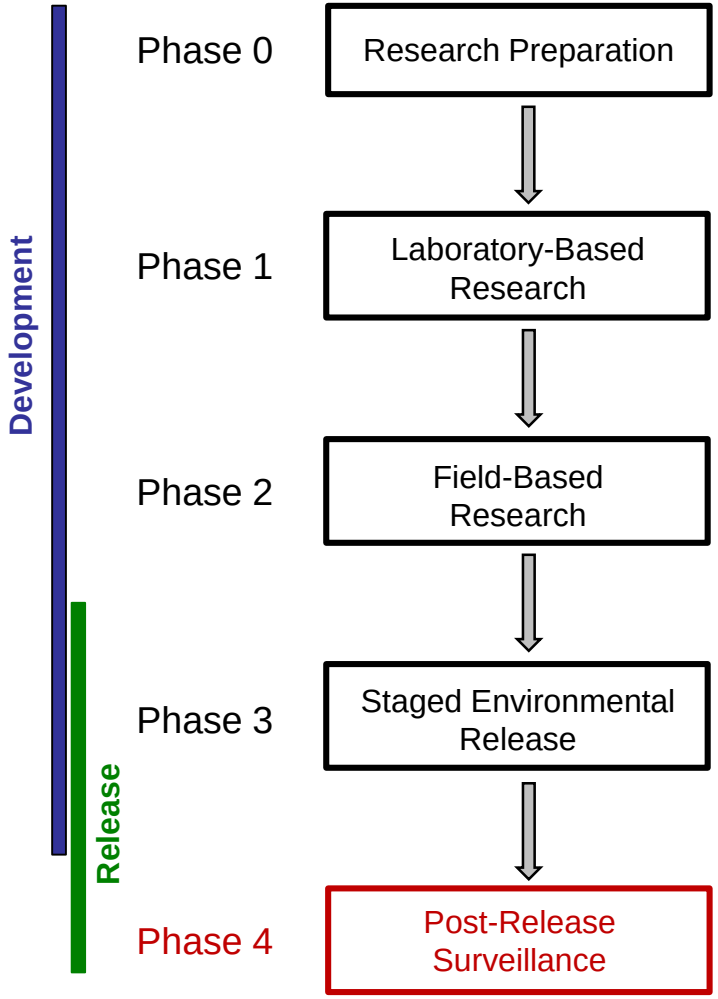


Phase 3.
Staged environmental release

- Efficacy
- Environmental harm

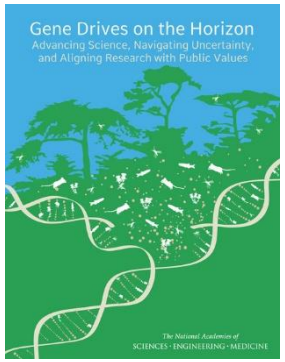


Development of a GD organism



Phase 4.
Post-release surveillance

- Measure impact

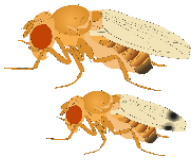


Development of a GD organism

Conditions to be met before a **GM insect with gene drive** is tested under less contained conditions

- Trait is stably expressed
- No unintended effects of the transformation detected
- GM insects are as fit/ competitive as wildtypes
- Gene drive works as intended under confined/ controlled conditions
- ……

Gene drives in *D. suzukii* - Status



- Embryonic lethal transgenes have been introduced into *D. melanogaster* *(Horn & Wimmer 2003)*
- Genome editing of *D. suzukii* is feasible – CRISPR-Cas9 system developed for *D. melanogaster* also funtions in *D. suzukii* *(Li & Scott 2016; Schetelig et al. 2018)*
- A *Medea*-drive system has succesfully been engineered into *D. suzukii* *(Buchman et al. 2018)*
  - inheritance rates of up to 100% observed
  - High release frequency required
  - rather large fitness costs leading to self-limiting dynamics of the system

Problem formulation

What do we not want to see harmed? What must be protected?

➡ *Protection goals*

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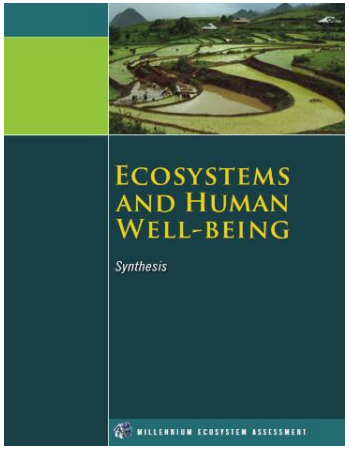
Gray (2012) Collection of Biosafety Reviews 6, 10-65

Protection goals



Policy protection goal: BIODIVERSITY

Millennium Ecosystem Assessment (2015)

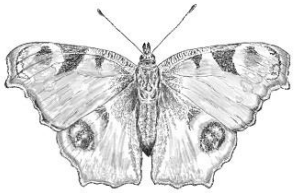
(conducted under the auspices of the United Nations)

Regulating services

- Biological control of arthropod pests
- Pollination

Cultural services

- Protected butterflies



Supporting services

- Nutrient cycling, decomposition

Devos et al. (2015) EMBO Reports 16, 1060-1063

Problem formulation

What do we not want to see harmed? What must be protected?

➡ *Protection goals*

Can we envision a way in which they could be harmed?

➡ *Pathway to harm*

How can we assess whether they are likely to be harmed?

➡ *Development of risk hypotheses and a plan to test them*

Gray (2012) Collection of Biosafety Reviews 6, 10-65

Plausible pathways to harm I

Release of GD *D. suzukii*

Biological control function is disrupted

Plausible pathways to harm I

Release of GD *D. suzukii*

Populations of *D. suzukii* are eradicated

Lack of hosts/ prey

Populations of natural enemies are reduced

Biological control function is disrupted

Plausible pathways to harm I

Release of GD *D. suzukii*

Natural enemies consume GD *D. suzukii*

GD trait is toxic

GD *D. suzukiii* have reduced prey/ host quality

Natural enemies are adversely affected

Populations of *D. suzukii* are eradicated

Lack of hosts/ prey

Populations of natural enemies are reduced

Biological control function is disrupted

Plausible pathways to harm I

Evidence available

- In invaded areas, *D. suzukii* is unlikely to become a key component in the food web
  - ➢ eradication has negligible indirect food-web effects

- In area of origin, highly specialized natural enemies occur that could be adversely affected
  (Nomano et al. 2017; Girod et al. 2018a,b)

Plausible pathways to harm II

Release of GD *D. suzukii*

↓

Hybridization with other native *Drosophila* spp.

Biological control function is disrupted

Plausible pathways to harm II

Release of GD *D. suzukii*

↓

Hybridization with other native *Drosophila* spp.

↓

Gene drives is functional

↓

Populations of *Drosophila* are eradicated

↓

Lack of hosts/ prey

↓

Populations of natural enemies are reduced

↓

Biological control function is disrupted

Plausible pathways to harm II

Evidence available

- Hybridization among *Drosophila* has been reported for closely related species, i.e. species within one species group – but it is a rare event *(Bock 1984; Garrigan et al. 2012)*

- Transfer of transposable elements has been reported
  - ➢ Example: P-element invaded *D. melanogaster* genome from *D. willistoni* *(Daniel et al. 1990)*

Non-plausible pathways to harm I

Release of GD *D. suzukii*

↓

Hybridization with other native *Drosophila* spp.

↓

Hybrids have increased fitness

↓

Outcompete native species

↓

Hybrids contain functional drive

↓

Populations decline

↓

Species contributes to bio-control

↓

Biological control function is disrupted

Evidence available:

- No *Drosophila* species known from the *D. suzukii* habitat that provides bio-control function

Non-plausible pathways to harm II

Release of GD *D. suzukii*

↓

Horizontal gene transfer to unrelated organism

↓

Gene drive is functional

↓

Species contributes to biological control

↓

Populations decline

↓

Biological control function is disrupted

Evidence available:

- Probability of HGT between *D. suzukii* and other unrelated organisms to occur is extremely unlikely under natural conditions
- Unlikely that drive is functional

Experience with insect control technologies

Insect control technologies are available that require the release (and establishment) of living organisms

- Classical biological control
  - Release of natural enemies from area of origin of the invasive pest
- Sterile Insect Technique (SIT)
  - Release of mass-produced sterilized insects
- Incompatible Insect Technique (IIT)
  - Release of insects carrying incompatible *Wolbachia* strains
- Genetically modified insects
  - Insects contain self-limiting traits

Conclusions

- Experience exists with pest control technologies that require the release/ establishment of living organisms
- Existing risk assessment frameworks can be used to assess GD organisms
- We see no novel risks with the use of GD organisms, but effects might be more severe
- The context in which the GD organisms are used is important
  - ERA needs to consider benefits (as for classical biocontrol)
  - What constituts harm needs to be defined

Thank you for your attention

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