Environmental Risk Assessment for Gene Drives

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ILSI RESEARCH FOUNDATION

ILSI Research Foundation

About Us

As a non-profit, public charitable organization, the ILSI Research Foundation collaborates with experts to respond to relevant issues that have a global impact through applied research, capacity building, education and outreach.

Our Work

All programs are for public benefit and focus on contributing to long-term solutions. This includes:

Sustainable Nutrition Security

Environmental Risk Assessment of Genetically Engineered Crops

Environmental Risk Assessment of Gene Drives

Genetically Engineered Food and Feed Safety Assessment

Biosafety Capacity Building

Contents of My Presentation

What is environmental risk assessment?

- How do we do it?
- How is it different from research science?

Description of a series of workshops and consultations involving problem formulation exercises

- Considering use of gene drives to reduce incidence of malaria
- VERY compressed summary of results
- Broad protection goals with relevance to this application of gene drives

Lessons learned and conclusions about gene drive risk assessment for other insects and applications

Environmental Risk Assessment for GE Insects

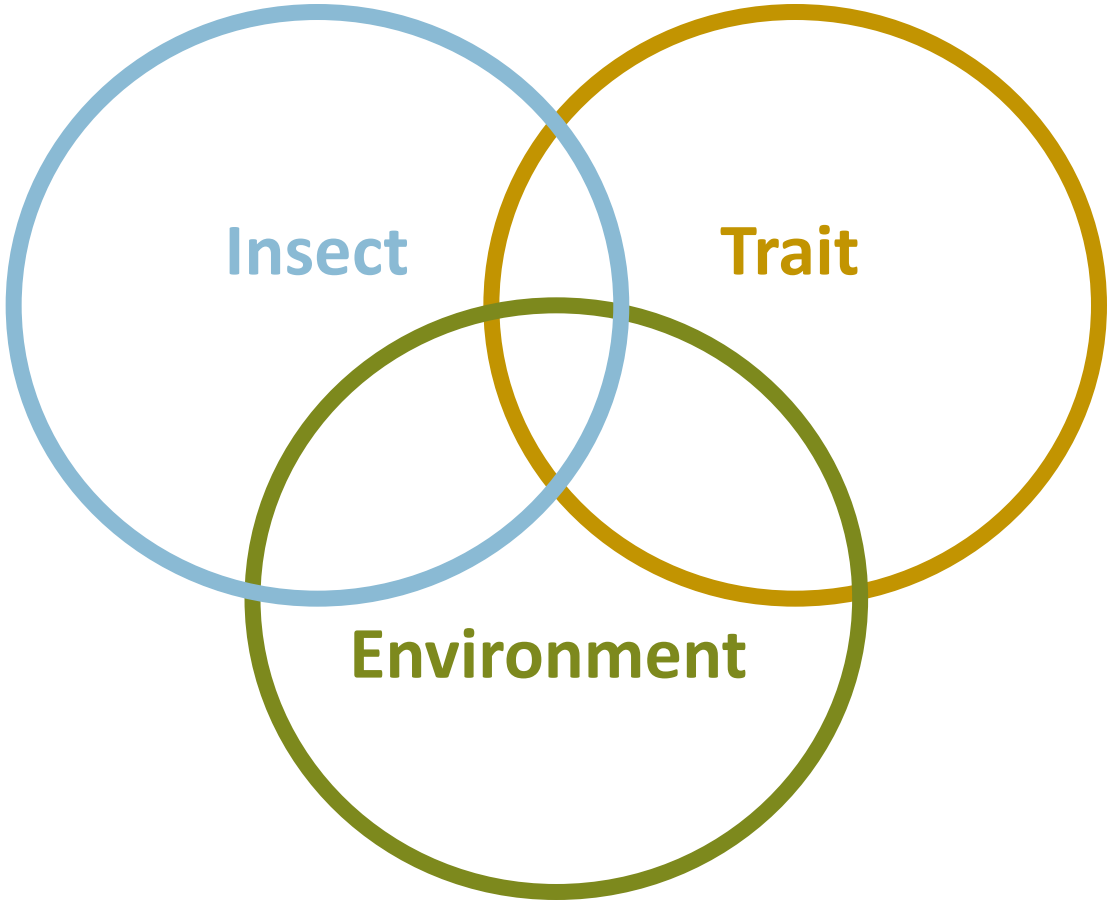
"Environment" in this case includes:

- Physical environment
- Biological environment (i.e. ecology)
- Human environment

Specific parameters to be considered for ERA usually are incorporated into laws and regulations

Risk assessment is "case specific"

- You can't do one for "all gene drive insects"



Is Risk Assessment a Science?

Risk assessment makes use of science

- Uses credible data
- Logical and rational examination of the real world

But the assessment itself is not purely science

- Doesn't generate "new" knowledge
- Incorporates judgments about relevance and significance of information
  - This is inseparable from the assessment

Risk assessment is not research!

- It is time sensitive, and is done to support decision making

Problem Formulation

"If I had only one hour to save the world, I would spend fifty-five minutes defining the problem, and only five minutes finding the solution."

-Albert Einstein (probably not)

Problem Formulation is the name given to a scoping process that typically involves:

- Identifying Broad Protection Goals
- Refining those broad protection goals to more specific protection goals you think are directly relevant to your case
- Identifying ways to measure the potential "harms" to

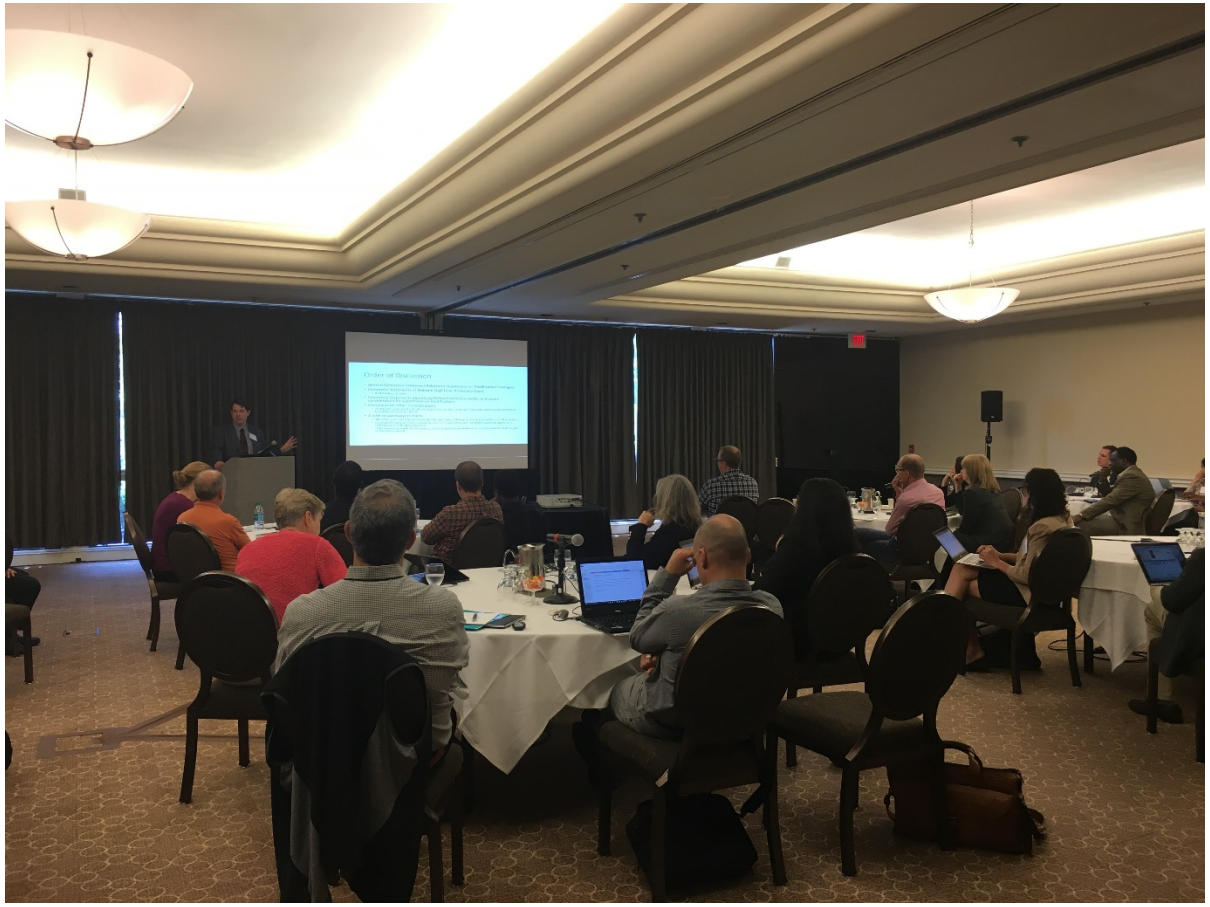
Five Workshops and Consultations Including Problem Formulation Exercises

Workshop

- Reston, Virginia, May 25-27, 2016

Consultations

- Accra, Ghana, Oct. 17-19, 2016
- Nairobi, Kenya, June 20-22, 2017
- Gabarone, Botswana June 26-28, 2017
- Libreville, Gabon, Feb. 20-22, 2018



Purpose of the Workshop and Consultations

To begin conversations about environmental or ecological risks that may be associated with the use of gene drive mosquitos for malaria control in Africa

To identify areas where researchers and development programs should be thinking about collecting data in support of risk assessment

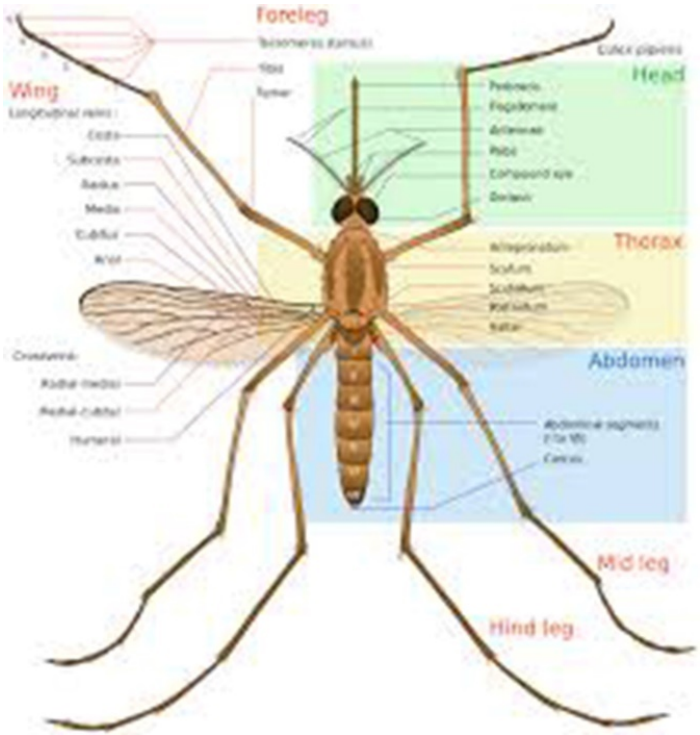
Provide a rational starting point for developers, researchers, and regulators to think about the use of gene drive technology for malaria control

Structure of the Workshop/Consultations

Day 1: Information to Inform Problem Formulation

Day 2: Breakouts using Hypothetical Case Studies

Day 3: Review and Discussion



Scientific & Technical Background → Breakout Groups → Review and Discussion

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Perspective Piece

Results from the Workshop "Problem Formulation for the Use of Gene Drive in Mosquitoes"

Andrew Roberts,[1]* Paulo Paes de Andrade,[2] Fredros Okumu,[3] Hector Quemada,[4] Moussa Savadogo,[5] Jerome Amir Singh,[6,7] and Stephanie James[8]

[1]*Center for Environmental Risk Assessment, International Life Sciences Institute Research Foundation, Washington, District of Columbia;* [2]*Department of Genetics, Federal University of Pernambuco, Recife, Brazil;* [3]*Ifakara Health Institute, Environmental Health and Ecological Sciences Thematic Group, Dar es Salaam, Tanzania;* [4]*Institute for International Crop Improvement, Donald Danforth Plant Science Center, Saint Louis, Missouri;* [5]*African Biosafety Network of Expertise, NEPAD Agency, Ouagadougou Node, University of Ouagadougou, Burkina Faso;* [6]*Centre for the AIDS Programme of Research in South Africa, University of KwaZulu-Natal, Durban, South Africa;* [7]*Dalla Lana School of Public Health, University of Toronto, Ontario, Canada;* [8]*Foundation for the National Institutes of Health, Bethesda, Maryland*

Abstract. Reducing the incidence of malaria has been a public health priority for nearly a century. New technologies and associated vector control strategies play an important role in the prospect of sustained reductions. The development of the CRISPR/Cas9 gene editing system has generated new possibilities for the use of gene-drive constructs to reduce or alter vector populations to reduce malaria incidence. However, before these technologies can be developed and exploited, it will be necessary to understand and assess the likelihood of any potential harms to humans or the environment. To begin this process, the Foundation for the National Institutes of Health and the International Life Sciences Institute Research Foundation organized an expert workshop to consider the potential risks related to the use of gene drives in *Anopheles gambiae* for malaria control in Africa. The resulting discussion yielded a series of consensus points that are reported here.

Consensus Points

Non-Pertinent Broad Protection Goals:

- Soil Quality
- Air Quality
- Natural Resources (other than biodiversity)
- Agricultural Production (excluding animal health)

Human Health

The relevant interaction for human health is biting

Proteins encoded by genes introduced into *Anopheles gambiae*, including components of the gene drive and markers, should be considered with respect to toxicity and allergenicity potential.

Horizontal gene flow to humans is extremely unlikely to occur.

Because *Anopheles gambiae* is an important disease vector, consideration should be given to potential alterations in disease transmission

Biodiversity

(General Consensus Statements)

Biodiversity

Anopheles gambiae is not a "keystone" species in the environment and is not known to provide any non-redundant ecosystem services

Anopheles gambiae interacts with other species by feeding on them, being consumed as prey, or competing with them.

Biodiversity (Refined harms and priorities for consideration)

Biodiversity

Anopheles gambiae is not known to be the sole or primary food source for any organism, with the possible exception of a few species of spider known to prefer Anophelines.

Removing *Anopheles gambiae* from the environment is unlikely to harm species that feed on it, due to the availability of other prey, including Anophelines.

- Birds, bats, fish etc.
- This is primarily relevant for suppression strategies

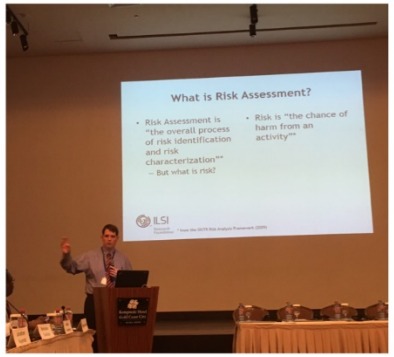
Consideration should be given to any proteins introduced into *Anopheles gambiae* (including gene drive components or markers) for toxicity to other species

Biodiversity (Gene Flow)

Gene flow to other species
within the *Anopheles gambiae* s.l. complex through hybridization is likely, and does not create additional pathways to harm.

Horizontal gene transfer is not likely to occur to other organisms on any relevant time scale and is not a pertinent pathway to harm


Camilla Beach
Elizabeth Williams
Andrew Roberts


What is Risk Assessment?
• Risk Assessment is "the overall process of risk identification and risk characterization""
– But what is risk?
• Risk is "the chance of harm from an activity""
ILSI


Gene Drives to Target Snails- A Case Study in Problem Formulation
ILSI

General Statement on Exposure Related to Species Specific Population Suppression And Population Alteration Strategies

Population Suppression

- Gene Drive Mosquitos for population suppression are designed to eventually reduce in numbers in the environment over a relevant time.

Population Alteration

- Gene Drive Mosquitos for population alteration are designed to persist in the environment over a relevant time.

Lessons Learned and Considerations for other Gene Drive Insects

We have experience with risk assessment for insects from biocontrol activities

Do not over-focus on the molecular genetics!

- 25+ years of ERA for GE plants suggest that this wastes a lot of time and energy while contributing very little to the risk assessment

Risk assessments for gene drive insects should be conducted in the context of current control activities

- Most of these insects are likely to be the target of control or eradication programs

Don’t focus on interesting research questions

Acknowledgments

I want to acknowledge the incredibly hard work of all the people participating in all of these events, although I can't possible name them all:

Colleagues at the ILSI Research Foundation

- John Teem (especially for slides), Libby Williams, Karin Christianson, and Layla Tarar

Foundation for the National Institutes of Health

Providing financial support to allow ILSI Research Foundation to be part of this work

New Partnership for African Development

- Initiating, organizing managing and hosting the consultations in Africa

Speakers at all five workshops

Participants in Reston, Ghana, Nairobi, Gabarone, and Libreville

Thank you!

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