TARGET
MALARIA

A Vector Control Research Alliance

Risk assessment frameworks for gene drive: A Target Malaria perspective

Geoff Turner, Imperial College London

West Africa Animal Biotechnology Workshop
July 23-25, 2018
Dakar Senegal

Who Are We? *A Vector Control Research Alliance*

INSTITUT DE RECHERCHE EN SCIENCES DE LA SANTE
IRSS
BP 7192 OUAGA TéL.: 25 36 32 15

MALI-USA
International Center for Excellence in Research (ICER)
FMPOS
FAST
NIH
NIAID
LMVR
LPD
RML
University of Bamako
Leishmaniasis
Filariasis
GIS/RS
Malaria
Tick Borne Diseases
Medical Entomology
Malaria Research and Training Center (MRTC-E)
Dept.of Vectors and Vector Borne Diseases

FOR GOD AND MY COUNTRY
UVRI

UNIVERSITY OF GHANA

Imperial College London

POLO GGB
GENOMICS · GENETICS · BIOLOGY

Keele UNIVERSITY

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

UNIVERSITY OF NOTRE DAME

UNIVERSITY OF CAMBRIDGE
Department of Genetics

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UNIVERSITY *of* WASHINGTON

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CURES START HERE

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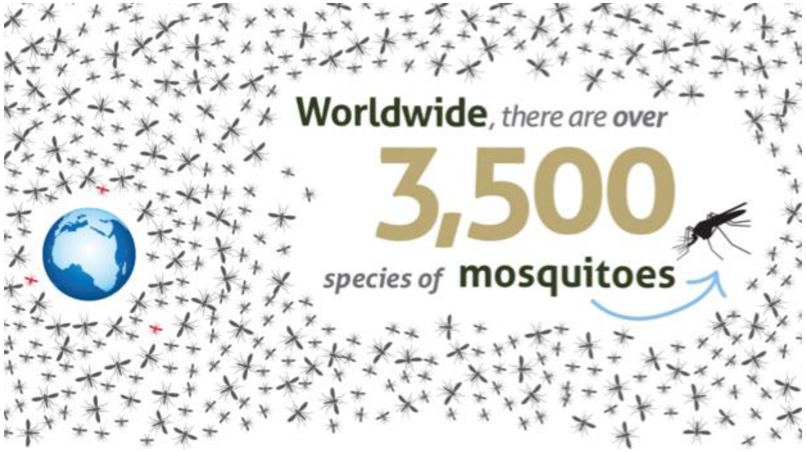
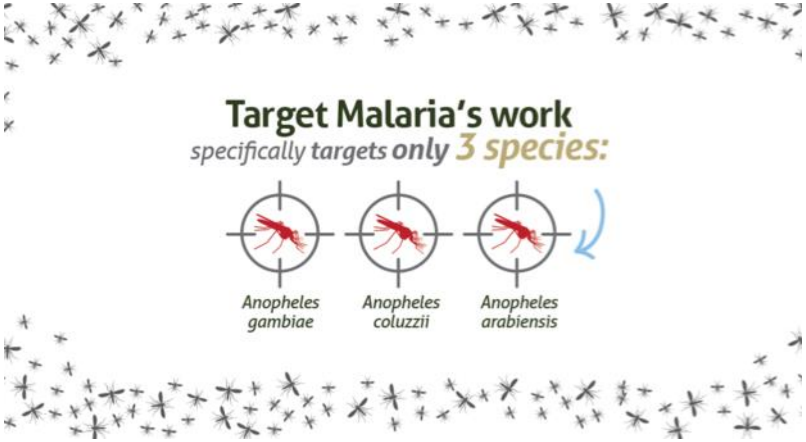
Malaria vector control- A targeted approach





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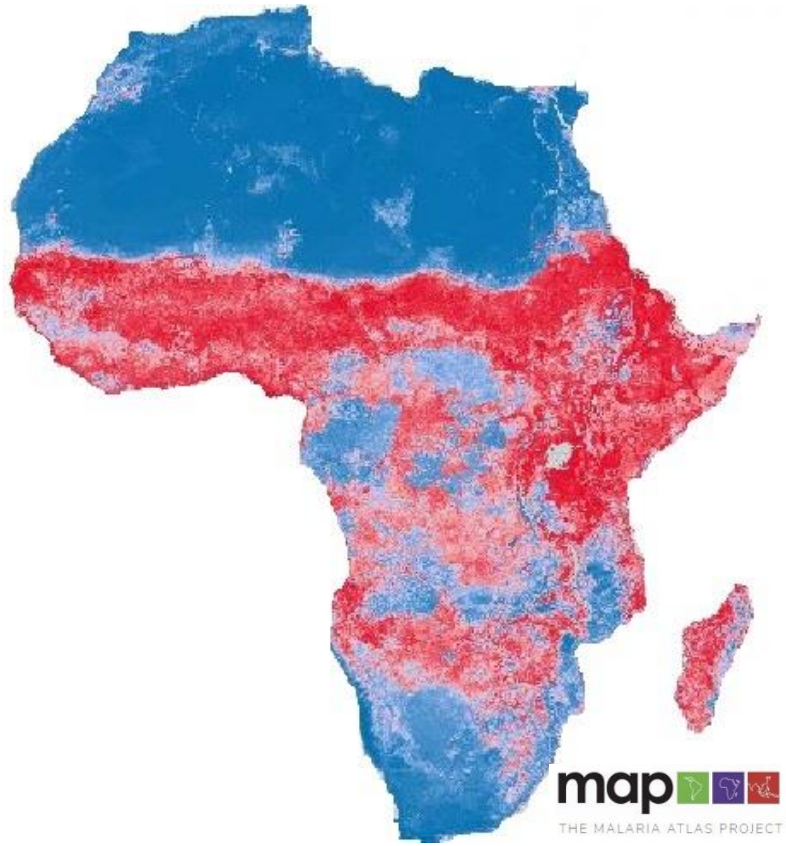
Target Malaria mission

- We will develop and share new, cost-effective and sustainable genetic technologies to modify mosquitoes and reduce malaria transmission
  - Complementary to existing methods
- Values
  - Excellence
  - Co-development
  - Evidence-driven
  - Open and accountable



Anopheles gambiae species complex distribution

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Program partners in Africa

Dr Abdoulaye Diabate
IRSS Bobo Dioulasso

Dr Mamadou Coulibaly
MRTC Bamako

Dr Jonathan Kayondo
UVRI Entebbe

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Ghana “Ecological Observatory” project

- Typical *Anopheles gambiae* habitat
- 4 year study-impacts of suppression
- Ecological community relationships
  - Larval niche and food web mapping
  - Plant/pollinator interactions
  - Microorganisms to large organisms
- DNA barcoding
- Methods development and transfer

UNIVERSITY OF GHANA

Representative sampling activities shown; images not taken during project specific activities in Ghana

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Built on three pillars

Science

Regulatory

Stakeholder engagement

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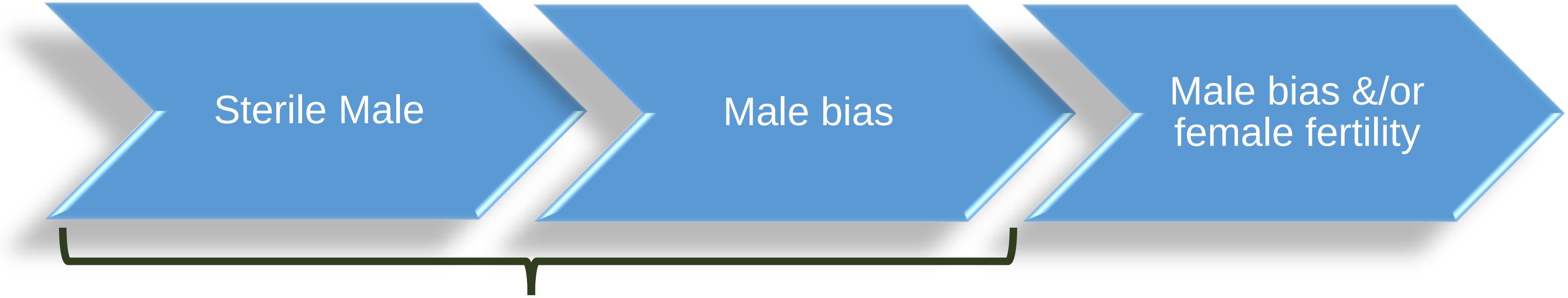
Science- Phased technology development



Self-limiting – No gene drive

- No intended impact on malaria

Self-sustaining- Gene drive

- No offspring
- No significant impact on mosquito population

- Male biased ratio in offspring
- Potential transient impact on mosquito population

- Targeting a long-term and sustainable impact on malaria-mosquito numbers

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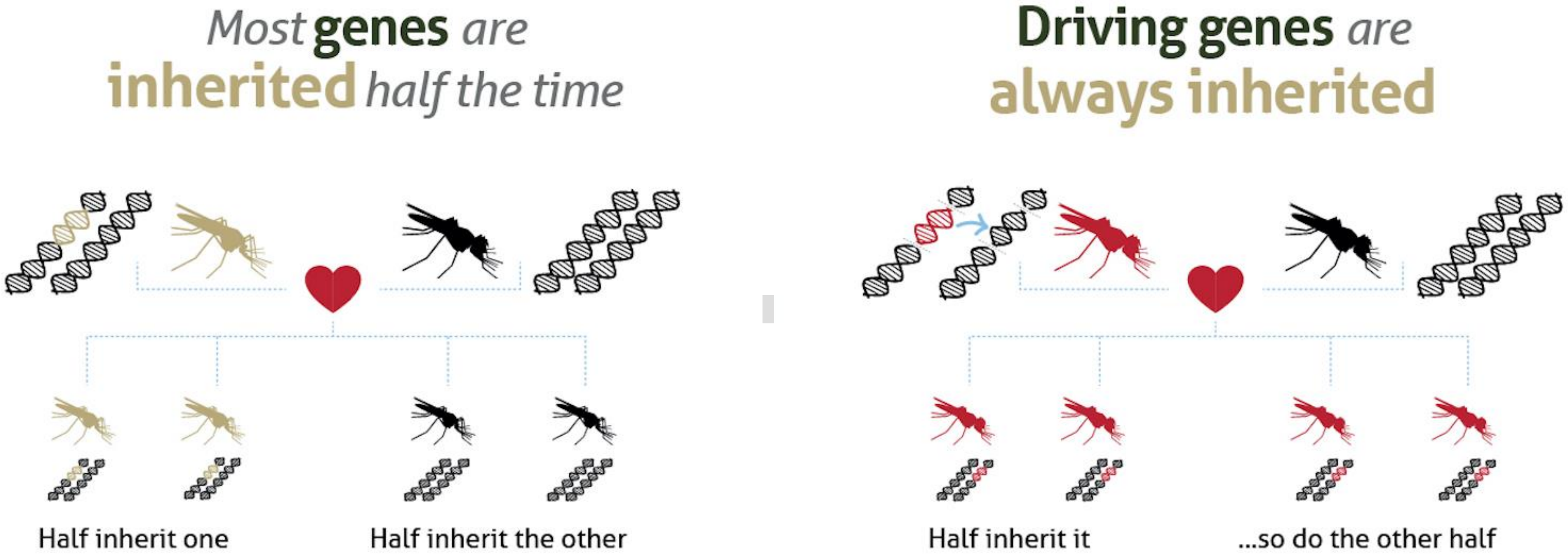
Science: What is gene drive?



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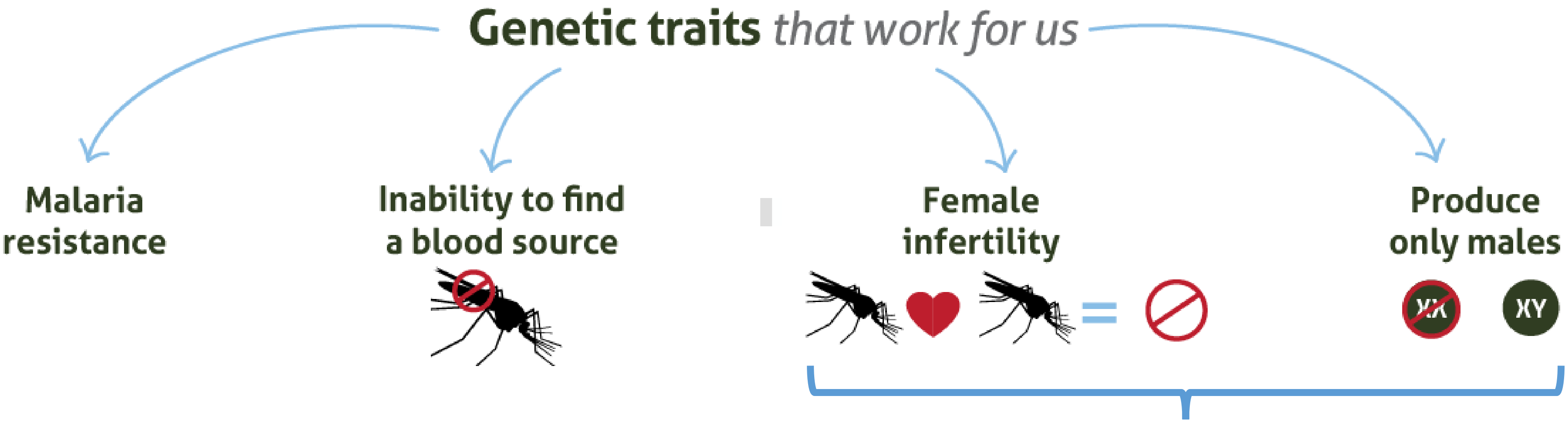
Science: What is gene drive?



Genetic traits *that work for us*

Malaria resistance

Inability to find a blood source

Female infertility

Produce only males

Population suppression

Stakeholder engagement; multi-layered

- International
- Africa regional
- National
- Regional
- Local

Different **stakeholder** groups

Different **levels** of acceptance needed

Different **tactics** and degrees of involvement

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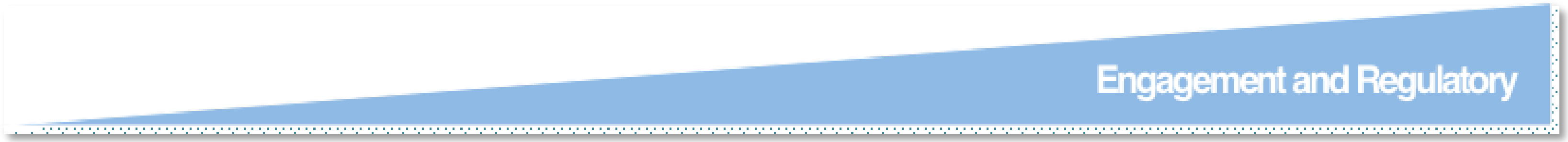
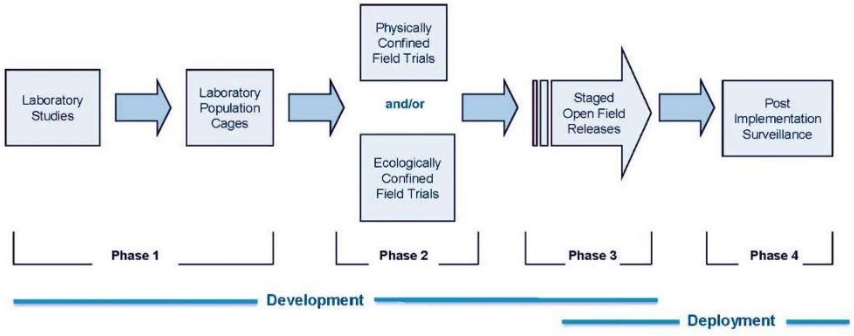
Regulatory-Pathway for evaluation

Contained laboratory experiments (London) → Large Cage experiments (Italy) → Additional Studies –off continent (USA) → Contained laboratory experiments in Africa → Small scale open field releases in Africa





WHO, 2014

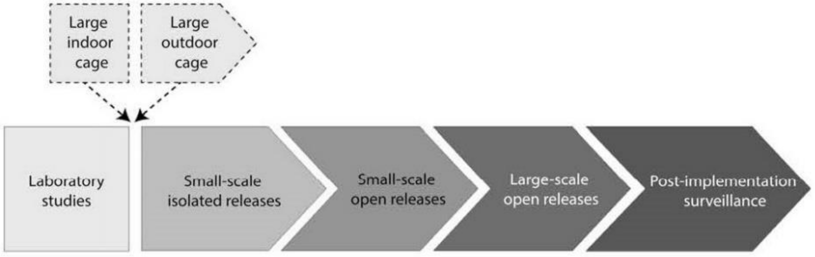


FIGURE 3. Pathway to deployment of gene drive mosquitoes.

James et al, 2018

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WHO Vector Control Advisory Group

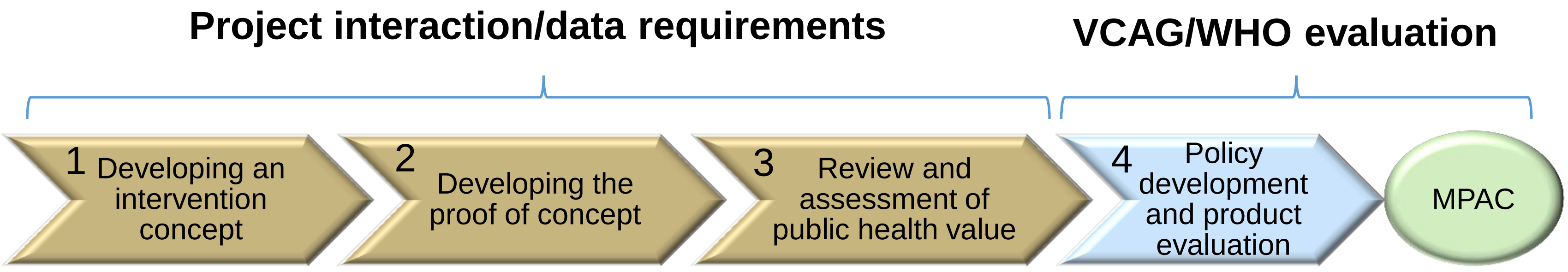
DESIGN
OF EPIDEMIOLOGICAL TRIALS FOR
VECTOR CONTROL PRODUCTS
REPORT OF A WHO EXPERT ADVISORY GROUP
CHÂTEAU DE PENTHES, GENE
24–25 APRIL 2017

Vector Control Advisory Group
MEETING REPORT
Eighth meeting of the WHO
Vector Control Advisory Group
World Health Organization

- Assess the public health value of new vector control product classes
- Staged technical framework with progressive evidence requirements

- Epidemiology
- Economics
- Technology dev’t pathway
- Manufacturability sustainability
- User compliance/acceptability

- Delivery and feasibility of implementation
- Regulatory/safety/ethical and environmental impact
- Target product profile description
- Policy/Strategy



Project interaction/data requirements

VCAG/WHO evaluation

1 Developing an intervention concept

2 Developing the proof of concept

3 Review and assessment of public health value

4 Policy development and product evaluation

MPAC

Biosafety assessment - Precedent for GM insects

Self-limiting – No gene drive

Sterile Male

Male bias

Small scale trials

Salud
MINISTERIO DE SALUD
PANAMÁ

comissão técnica nacional
CTNBio
de biossegurança

→ *Commercial scale*

BERSEKUTU BERTAMBAH MUTU

DEPARTMENT OF ENVIRONMENT
CAYMAN ISLANDS GOVERNMENT

FDA
Center for Veterinary Medicine

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Island wide

“Effectively” sterile

Small scale trials

comissão técnica nacional
CTNBio
de biossegurança

USDA

Female lethal/males survive

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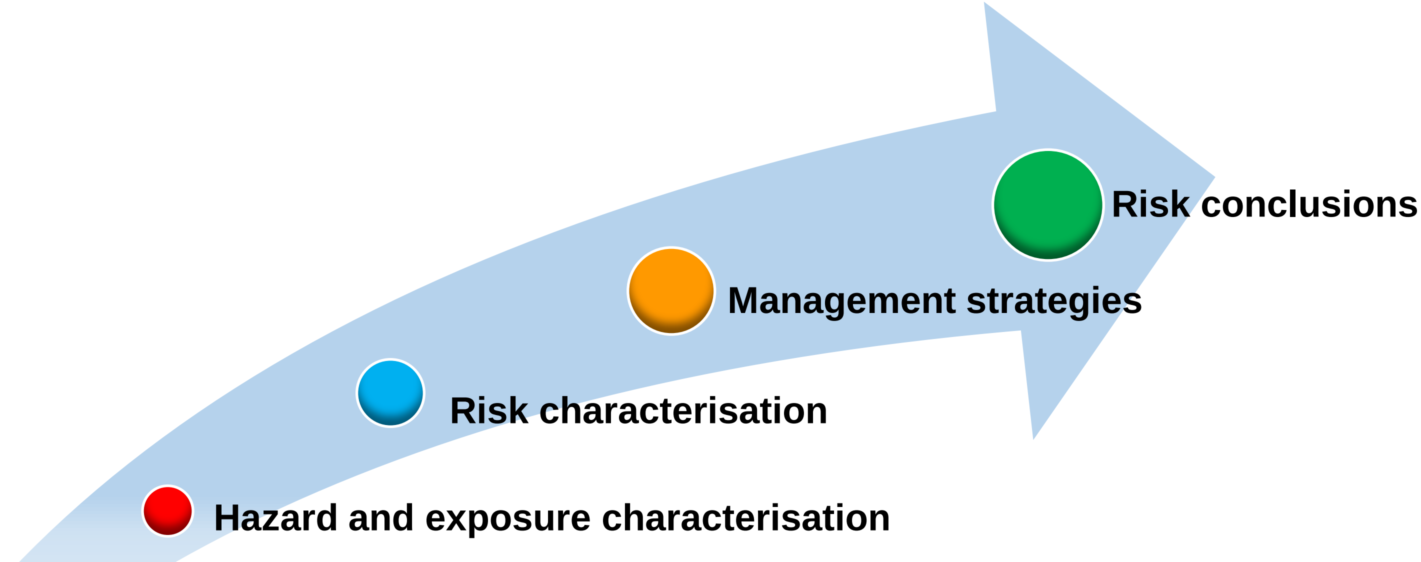
Biosafety assessment approach



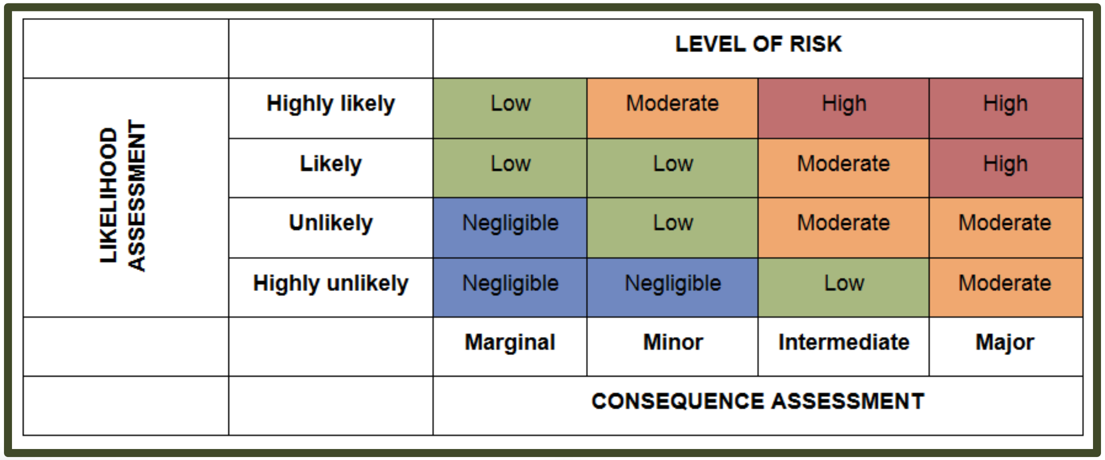
Risk conclusions

Management strategies

Risk characterisation

Hazard and exposure characterisation

Problem formulation



		LEVEL OF RISK			
LIKELIHOOD ASSESSMENT	Highly likely	Low	Moderate	High	High
	Likely	Low	Low	Moderate	High
	Unlikely	Negligible	Low	Moderate	Moderate
	Highly unlikely	Negligible	Negligible	Low	Moderate
		Marginal	Minor	Intermediate	Major
		CONSEQUENCE ASSESSMENT			

Australian Government, Department of Health and Ageing, Office of the Gene Technology Regulator. Risk Analysis Framework, 2013.

Technical guidance for risk assessment risk management

Self-Sustaining- Gene Drive

Intended to spread and persist

JOURNAL OF BIOLOGICAL CONTROL

Biological Control

INTERNATIONAL ORGANIZATION for BIOLOGICAL CONTROL of Noxious Animals and Plants

History of the first 50 Years (1956-2006)

Biological Control

Ecology and Applications

George E. Heimpel and Nicholas J. Mills

with a foreword by Jacques Brodeur

efsa

European Food Safety Authority

Convention on Biological Diversity

OECD

ASTMH

AMERICAN SOCIETY OF TROPICAL MEDICINE & HYGIENE

ADVANCING GLOBAL HEALTH SINCE 1903

World Health Organization

TDR For research on diseases of poverty

UNICEF • UNDP • World Bank • WHO

VOLUME 18, NUMBER 7 • JULY 2018 • ISSN 1530-3667

Vector-Borne and Zoonotic Diseases

Editor: Stephen Higgs, PhD, FRES, FASTMH

ASTMH

THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE

official Journal of the American Society of Tropical Medicine and Hygiene

Pathway to Deployment of Gene Drive Mosquitoes as a Potential Biocontrol Tool for Elimination of Malaria in Sub-Saharan Africa: Recommendations of a Scientific Working Group

TIME

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Emerging policy guidance

National academies of science

Gene Drives on the Horizon
Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values

Australian Academy of Science
DISCUSSION PAPER
SYNTHETIC GENE DRIVES IN AUSTRALIA: IMPLICATIONS OF EMERGING TECHNOLOGIES
AUSTRALIAN ACADEMY OF SCIENCE MAY 2017

European Academies
easac
Science Advisory Council
Genome editing: scientific opportunities, public interests and policy options in the European Union
Science Advice for the Benefit of Europe

National / Regional policy

HOUSE OF LORDS
Science and Technology Select Committee
1st Report of Session 2015–16
Genetically Modified Insects

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport
Gene drives
Policy report
RIVM Letter report 2016-0023
J. Westra et al.

GENE DRIVES
FOR MALARIA CONTROL AND ELIMINATION IN AFRICA
African Union
NEPAD
TRANSFORMING AFRICA

Haut Conseil des Biotechnologies
SCIENTIFIC COMMITTEE
SCIENTIFIC OPINION
in response to the referral of 12 October 2015 concerning use of genetically modified mosquitoes for vector control[1]
Paris, 31 May 2017

Emerging themes for risk assessment

- Socio-economic impact assessment
- Ecological quantitative risk assessment

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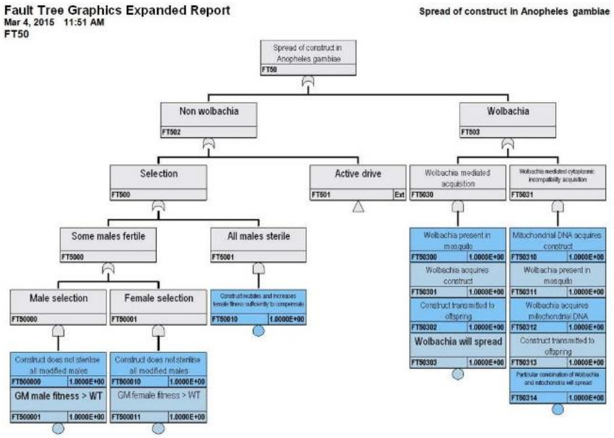
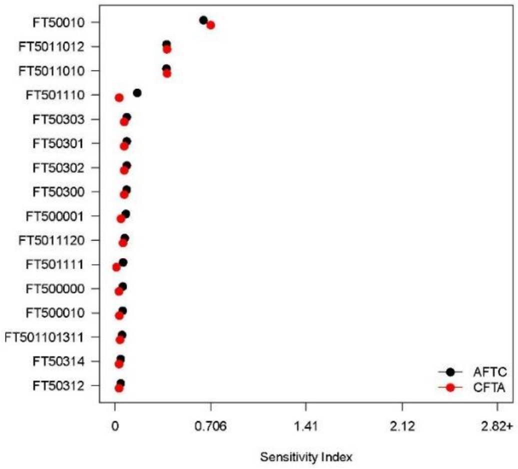
Tools for quantitative ecological risk assessment

Fault tree analysis*



Base event sensitivity*

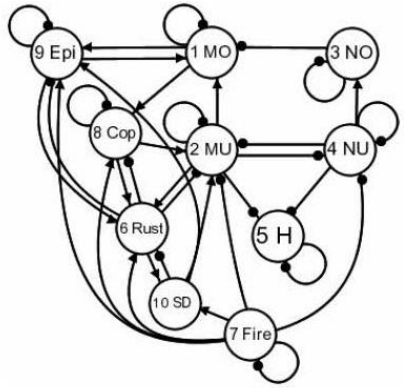


Mathematical modelling*

$$P\left(\mathcal{R}_0^G > \mathcal{R}_0^W\right) = P\left(\frac{a^{G^2} b_{xy}^G b_{yx}^G m e^{-\mu^G n^G}}{r\,\mu^G} > \frac{a^{W^2} b_{xy}^W b_{yx}^W m e^{-\mu^W n^W}}{r\,\mu^W}\right)$$

$$= P\left(\frac{a^{G^2} b_{xy}^G b_{yx}^G e^{-\mu^G n^G}}{\mu^G} > \frac{a^{W^2} b_{xy}^W b_{yx}^W e^{-\mu^W n^W}}{\mu^W}\right),$$

Signed digraphs**



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* Hayes *et al,* 2015 - Risk Assessment for Controlling Mosquito Vectors with Engineered Nucleases: Sterile Male Construct, Final Report. CSIRO Biosecurity Flagship, Hobart, Australia

** Dambacher *et al,* 2007 - Qualitative modelling and Bayesian network analysis for risk-based biosecurity decision making in complex systems. Australian Centre of Excellence for Risk Analysis

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Social, economic and public health impact assessment

Identification of key indicators

- National legislation
- International standards of best practice
- Emerging guidance

Data collection and field work

- Publically available data
- Semi-structured key informant interviews
- Participatory activities
- Village spatial and social organisation.

Outcomes

- Potential for impact
- Identification of benefits
- Site suitability assessment
- Identification of information gaps
- Management options

Consequence

Likelihood	Critical	High	Moderate	Low	Low	Moderate	High	Critical	
Highly Likely	4	4	3	2	2	3	4	4	Highly Likely
Probable	4	3	2	1	1	2	3	4	Probable
Unlikely	4	3	2	1	1	2	3	4	Unlikely
Very unlikely	3	2	1	1	1	1	2	3	Very unlikely

Opportunity ← → Risk

Building a comprehensive impact assessment framework

Established tools and guidance- Risk assessment and management

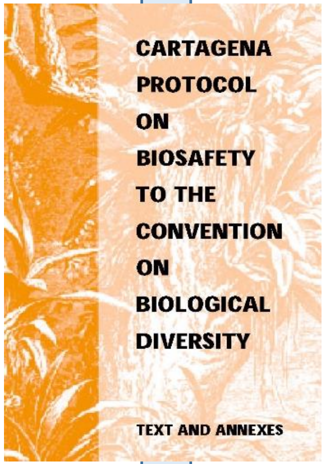
European Food Safety Authority

OECD

ASTMH

Guidance framework for testing of genetically modified mosquitoes

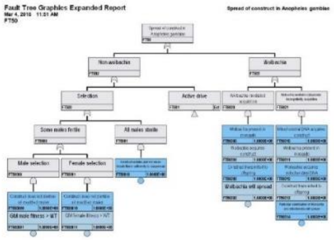
International obligations and national laws



CARTAGENA
PROTOCOL
ON
BIOSAFETY
TO THE
CONVENTION
ON
BIOLOGICAL
DIVERSITY

TEXT AND ANNEXES

New tools for biosafety assessment -Quantitative



New areas of assessment- Socioeconomic

Likelihood	Critical	High	Moderate	Low	Low	Moderate	High	Critical	
Highly Likely	4	4	3	2	2	3	4	4	Highly Likely
Probable	4	3	2	1	1	2	3	4	Probable
Unlikely	4	3	2	1	1	2	3	4	Unlikely
Very unlikely	3	2	1	1	1	1	2	3	Very unlikely

Emerging policy

African Union

NEPAD
TRANSFORMING AFRICA

- Global and national compliance
- Dynamic and responsive
- Accessible and transparent

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Acknowledgements

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BILL & MELINDA
GATES *foundation*

Open
Philanthropy
Project

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Thank you