



SAFE GENES

LEEDR Leaders Series

Wednesday, July 19, 2017



LEEDR Leaders Series

- Purpose: To share and disseminate innovative ideas, issues, and initiatives relevant to Safe Genes
- Schedule:
 - Ad hoc presentation series
 - Anticipate quarterly to semi-annually but flexible based on topics and timeliness
- Participation:
 - Not mandatory
 - Open to researchers in the Safe Genes community
- Upcoming anticipated events:
 - Guidance on Biosafety and IBCs for Gene Drives with Zach Adelman
 - Community Engagement Learning Platform with Jim Lavery
- Please send suggestions for future speakers or topics. (lianne.parr.ctr@darpa.mil)



Stakeholder engagement: an essential pillar for innovation

Presentation to DARPA and the Safe Genes project

Delphine Thizy, July 2017



Introduction to Target Malaria

Malaria: the problem

The burden:

- More than 200 million infections & half million deaths each year, ~90% in Africa, mostly the poor, mostly infants & children
- Economic losses in Africa ~\$12 billion a year

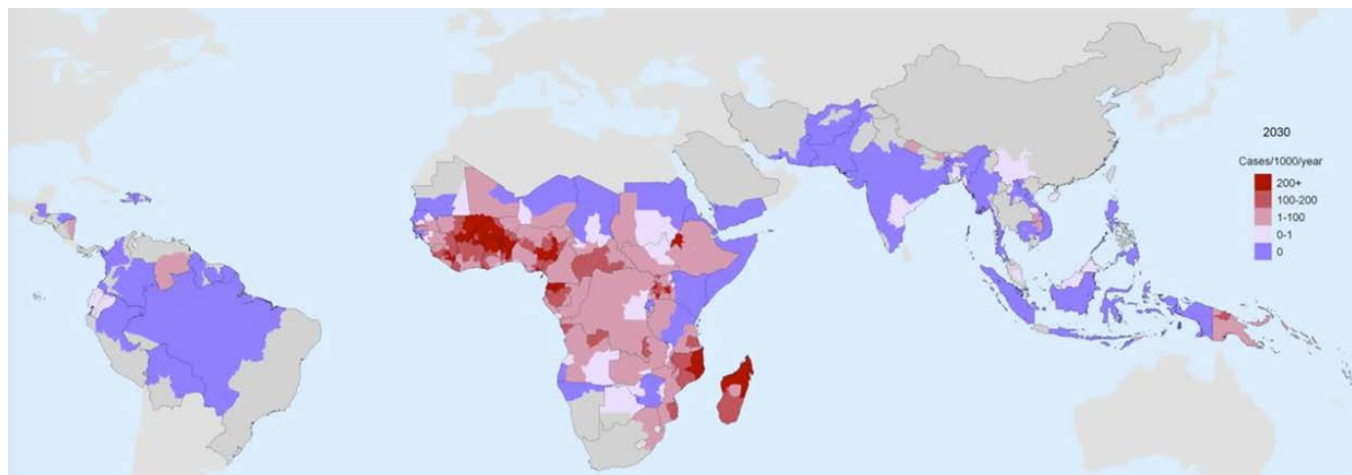
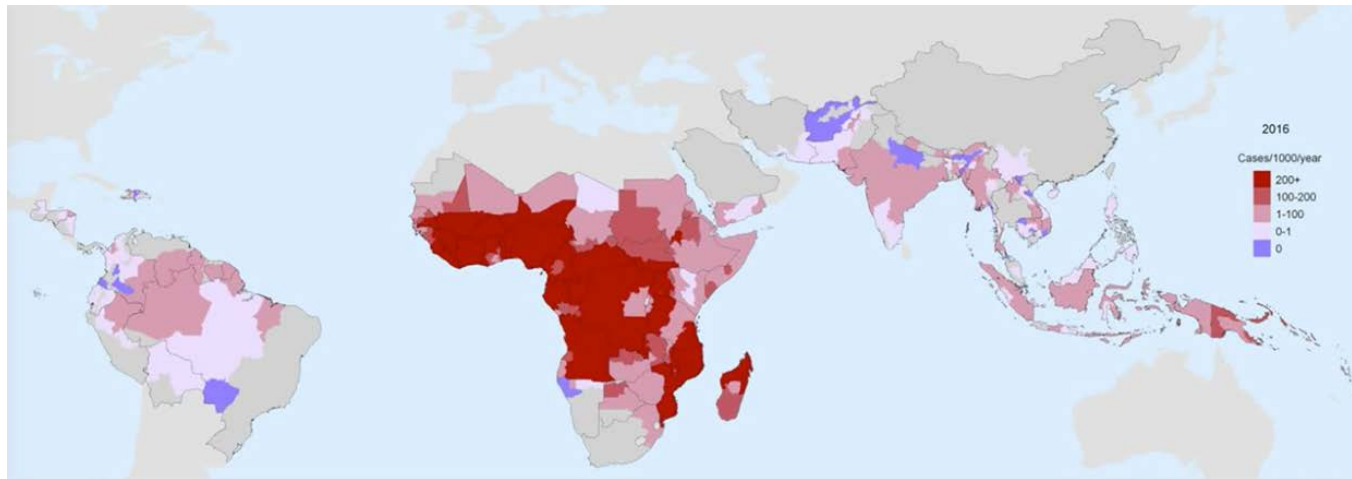
The biology:

- Malaria is caused by a parasite called *Plasmodium*
- In Africa most transmission is by 3 closely related species (*Anopheles gambiae*, *Anopheles coluzzii* and *Anopheles arabiensis*), plus *Anopheles funestus*
 - There are ~3500 species of mosquito, the vast majority of which do not transmit malaria
 - Other species can be important in specific locations
- Only female mosquitoes bite and only those infected can transmit the parasite

Extrapolating use of current interventions

WHO Global Technical Strategy (2016-2030)

Geographical distribution of *Plasmodium falciparum* malaria under the most optimistic scenario between 2015 and 2030 (with increase up to 9 billion USD/year) - Griffin et al., 2016



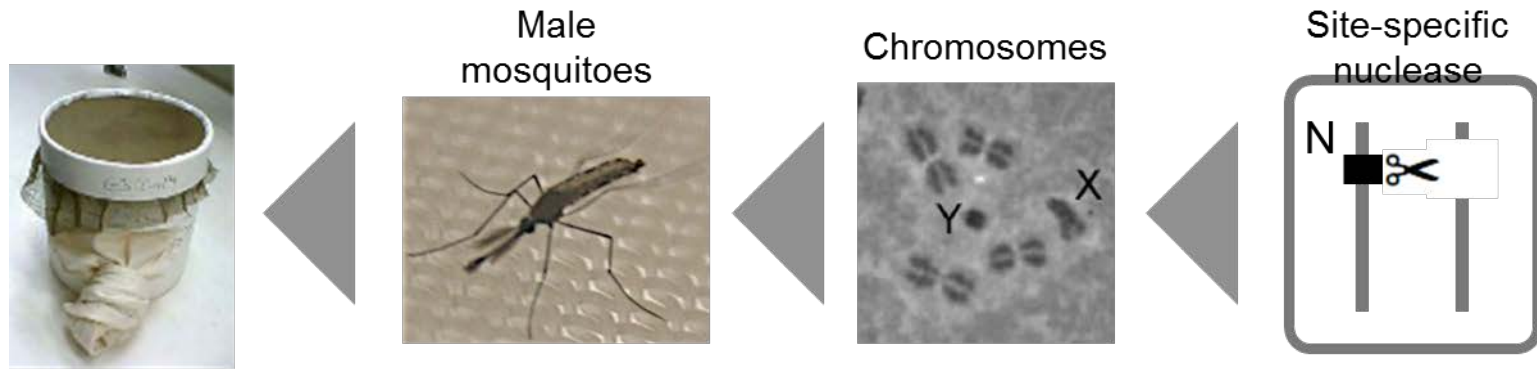
Target Malaria: who we are

- A not-for-profit research consortium, including:
 - Scientists: protein engineers, molecular biologists, medical entomologists, population biologists, and social scientists
 - Risk, regulatory and stakeholder engagement advisors
- With teams from Africa, Europe, and North America
- Working on a unique way to reduce malaria transmission by modifying mosquitoes from the target vector populations
- That will be freely licensed for use by authorities in countries where it has been approved

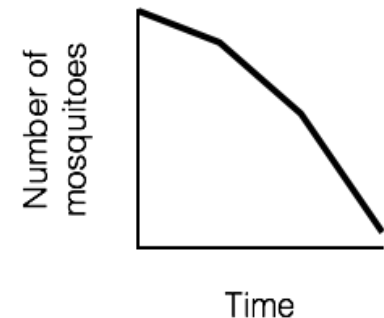
Our objectives

- To develop a novel genetic technology for vector control of *Anopheles* mosquitoes to contribute to a reduction in the burden of malaria in Africa
- An approach which is complementary to existing methods, sustainable, long term, and cost-effective
- To develop modified mosquitoes with a gene drive mechanism that would allow to reduce vector population in a relevant timeframe

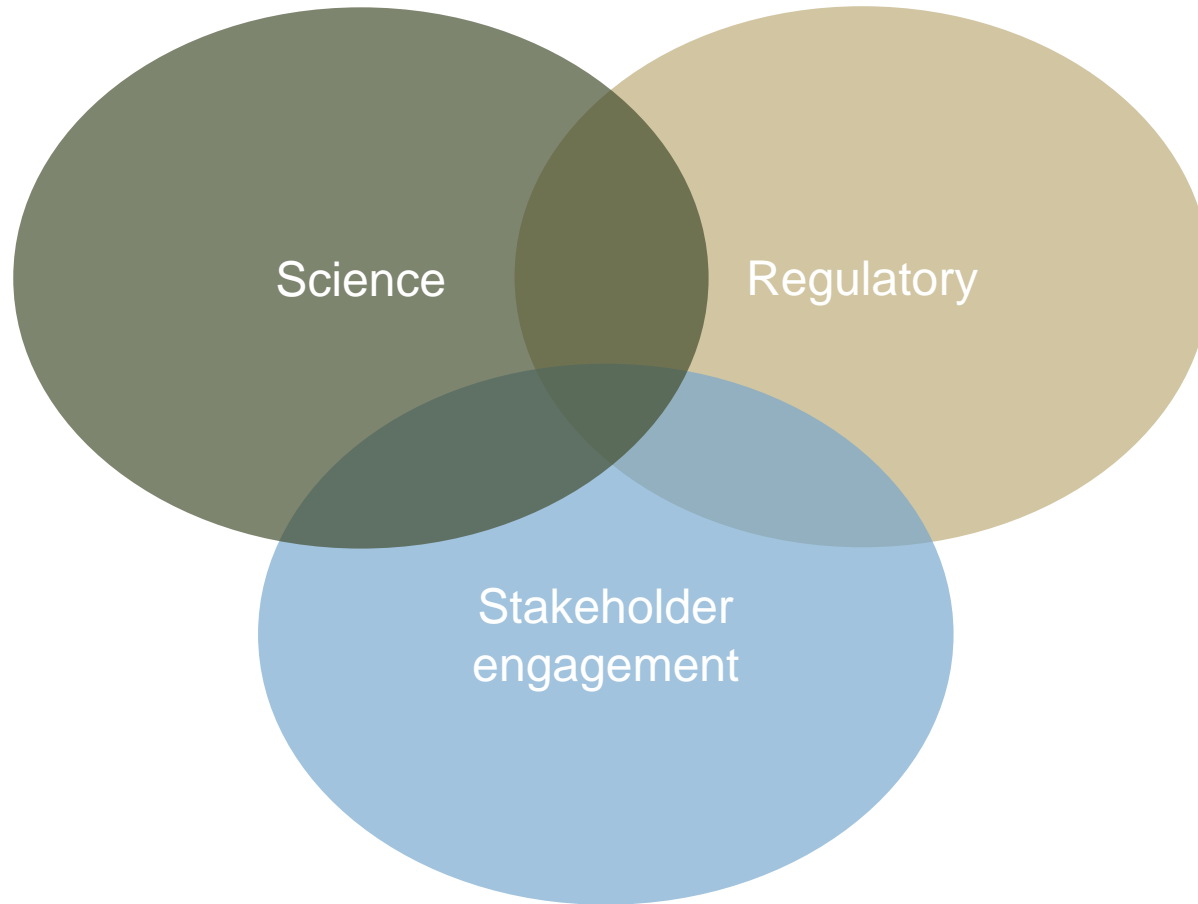
What would it look like?



- The product is a bucket of male mosquitoes carrying a gene coding for a sequence-specific DNA-cutting enzyme (nuclease)
 - Constructs will spread through the target population over time, and suppress the population as they do so.
- Reducing the number of mosquitoes will reduce malaria transmission (vectorial capacity).
- Reductions in vectorial capacity can be used to (a) reduce the burden of disease, and (b) facilitate elimination programmes



Built on three pillars





Stakeholder engagement strategy

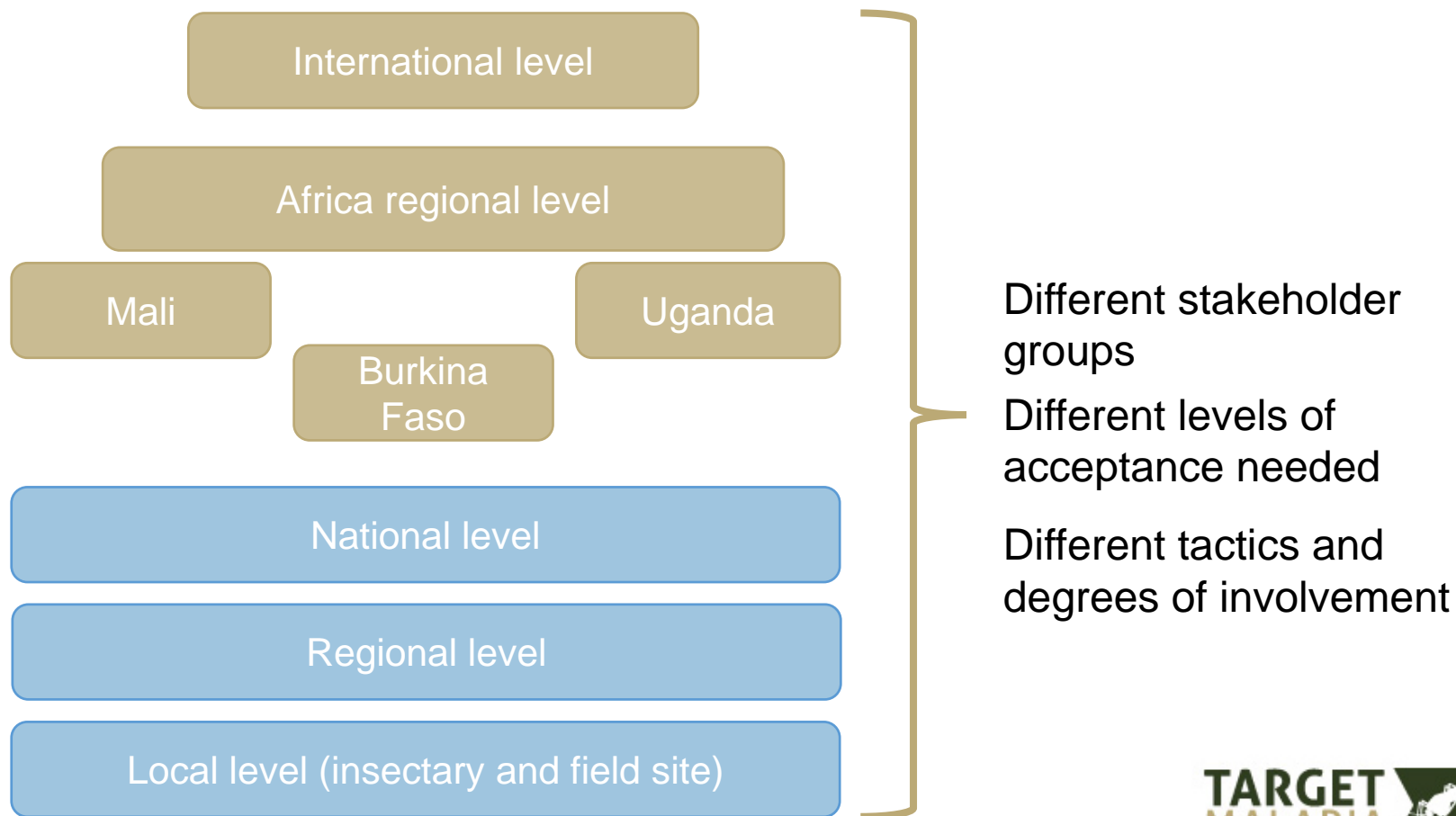
Objective of stakeholder engagement

- Reach consent for entomological collections requiring individual consent or community acceptance;
- Ensure acceptance for our approach;
- Gather public knowledge that can inform the project;
- Co-develop this technology with the different stakeholders;
- Take public inputs into consideration for risk management;
- Demonstrate the accountability of the project – e.g. grievance mechanisms. This is to ensure that all complaints from stakeholders can be addressed in a transparent and systematic way.

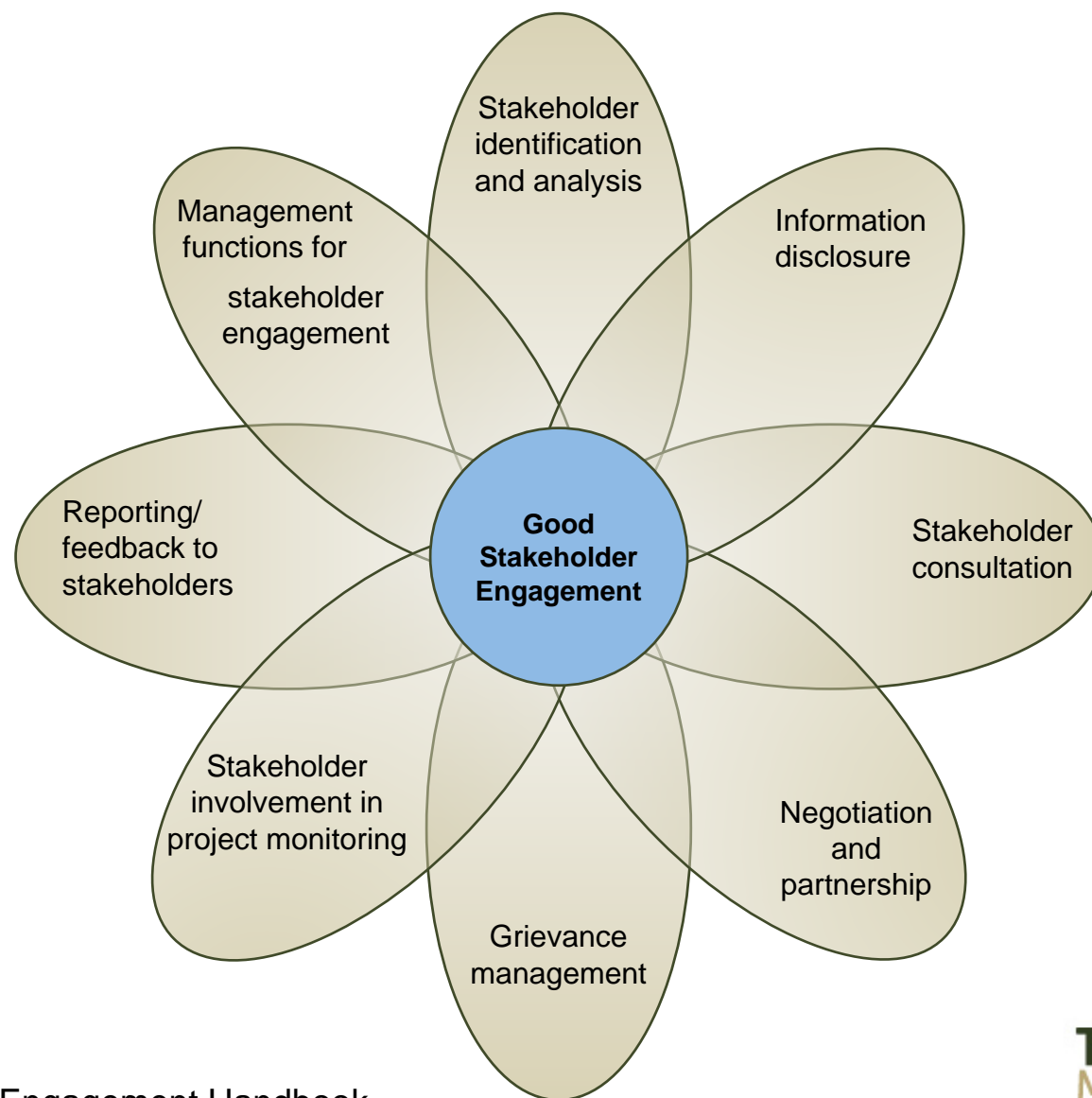
From engagement to co-development

- Target Malaria is committed to engagement:
 - Dedicated team & budget
 - Acceptance as a pre-condition for next steps of activities
- Engagement is usually focused on acceptance only
 - “Knowledge-deficit model”
 - “Educating” stakeholders about an existing technology
- Target Malaria has a co-development engagement model
 - Engaging during technology development
 - Engagement stakeholders about their knowledge
 - Feeding back this knowledge to the project to support co-development of the technology

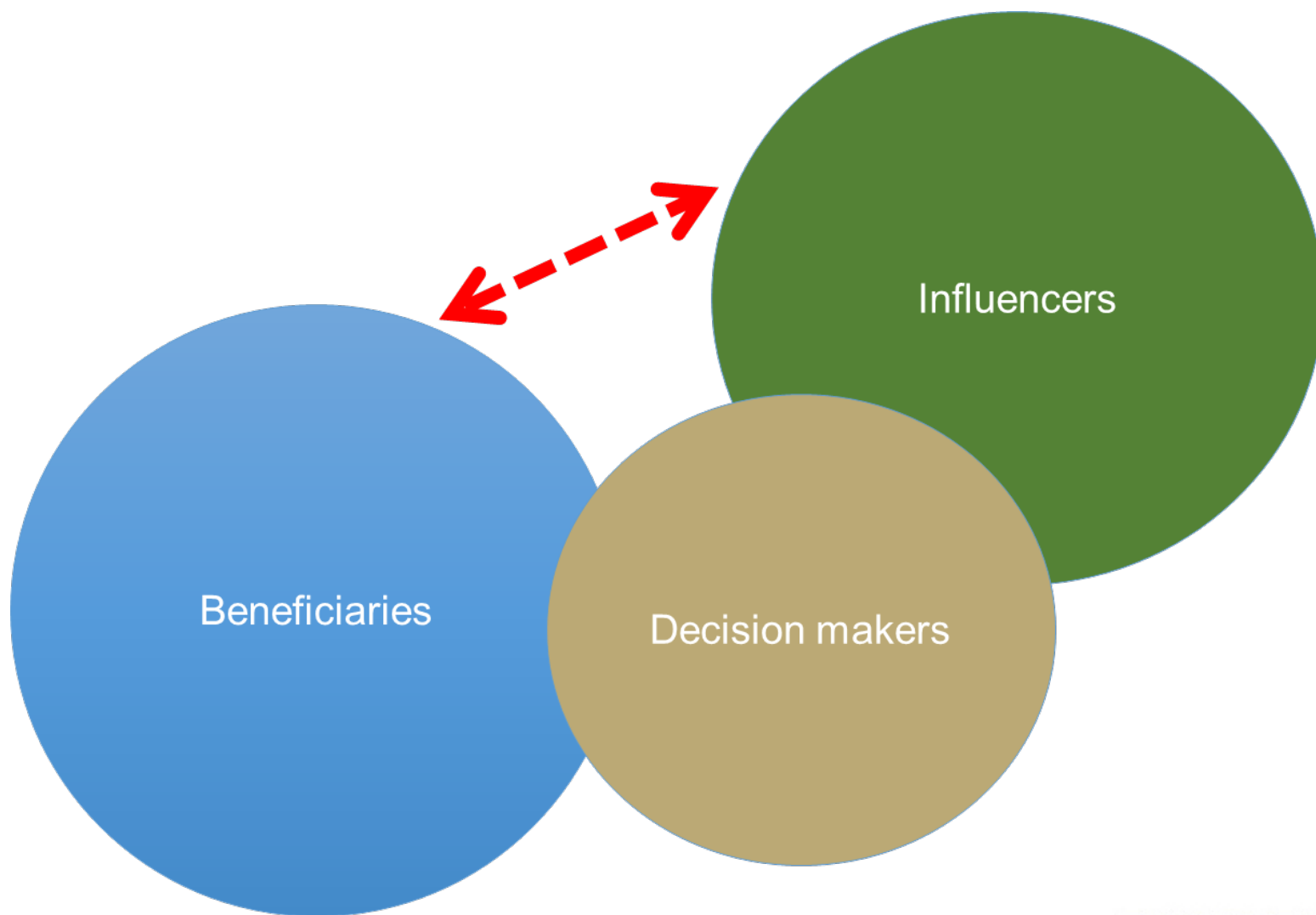
A multi-layered strategy



A multi-component approach



Key challenges: Audiences



Engagement challenges

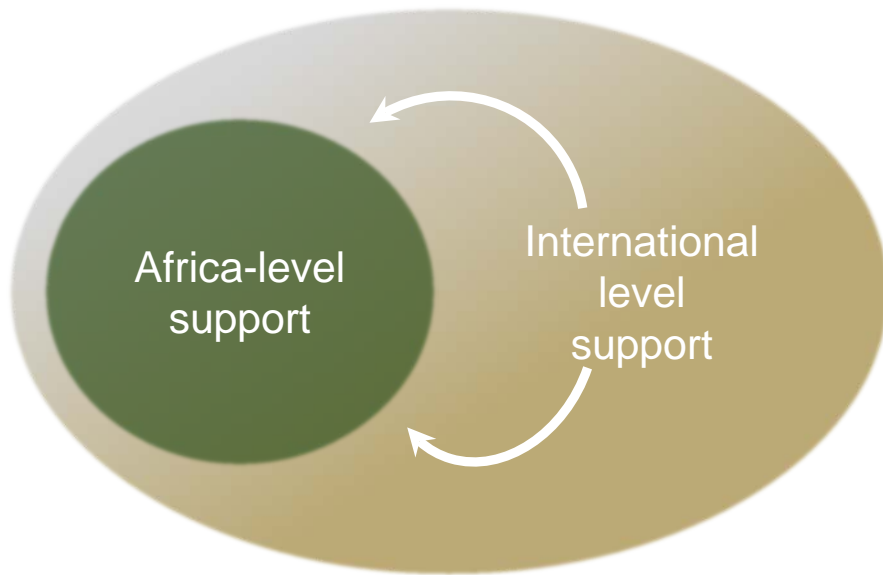
Overall the key challenges are:

- To identify key stakeholders to engage
- To bring and maintain the debate closer to those who could benefit from the technology,
- To find the right balance between engaging proactively and in a timely fashion, and not overpromising while the technology is still being developed,
- To enable informed decision-making,
- To open an informed discussion on risks and benefits
- Ensure stakeholders are being heard when they express their knowledge and inputs for the project's development
- To ensure that stakeholders understand that this isn't a silver bullet



Pan-African and global
engagement

Stakeholder Engagement Objectives



- Long-term objective: build acceptance for Target Malaria's technology in Africa
- Acceptance in Africa needs support outside of Africa too
- Not simply for the project but for the approach as a whole (gene drive)
- Need to support day to day work of the project AND the long term acceptance of the project – mutually supportive but not always the same

International level priorities

Malaria
scientific
experts &
researchers

Development
Donors/funders

Malaria policy
influencers

Other groups
involved in
novel vector
control
research

Environmental
groups

Global
'regulators'
and
regulation
influencers

Main objective

Need to be aware of
and understand the
technology &
approach of the
project

Build consensus on
best practices for
research & SE for
gene drive/novel
vector control tech

Identify concerns and
knowledge that can
help co-develop the
project

Regional level

Similar priority groups to the international level but Africa focused

Engagement with regulatory authorities (regulators, NEPAD, etc.)

Other policy makers (health authorities, etc.)

African scientists

African environmental groups

African broader public

Overall objective:
Need to be aware of and understand the technology & approach of the project

Identify concerns and knowledge that can help co-develop the project

Identify 'next generation' scientists and project partners

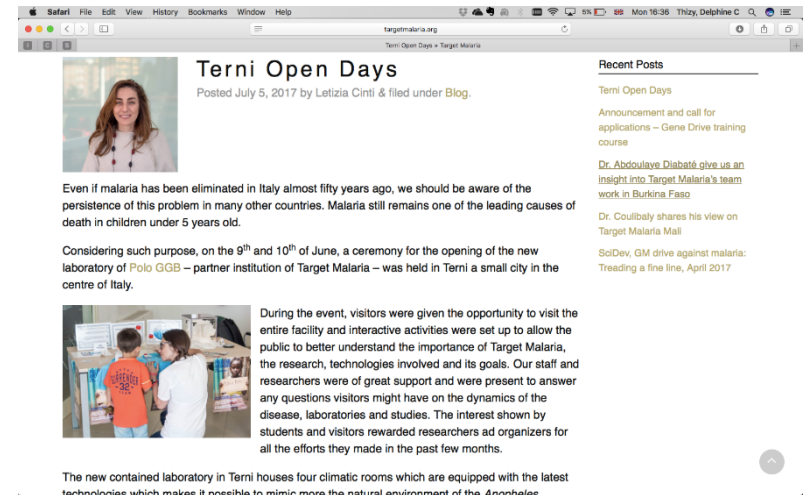


A Vector Control Research Alliance

Some results

In partner countries

- Social license to operate in the different villages where entomological collections take place
- Social license to operate for the containment facilities with support from the local communities
- Regulatory and local acceptance for the 1st importation and contained use of a genetically modified mosquito (sterile male strain – no gene drive) in Burkina Faso in Nov. 2016
- Good feedback from stakeholders for new containment facility in Italy



At global level

- Good engagement with regulators in Europe with several initiatives and in Africa with workshops organised by NEPAD
- Collaborative relationship with WHO
- Contributed to:
 - Mobilisation of researchers to respond to the call for moratorium on gene drive research
 - Providing evidence-based information to parties during CBD
 - Mobilisation of researchers for the CBD online forum

Open Letter on Gene Drive Technology

December 5, 2016

To the Parties to the Convention on Biological Diversity and the Parties to the Cartagena Protocol on Biosafety:

We urge you to support ongoing and new gene drive research, building on cautious and responsible practices and broad stakeholder dialogue.

The potential for gene drive technology is very significant. It is a novel tool which may enable interventions that are durable, cost-effective, and highly efficacious, complementing existing efforts to improve human health and environmental sustainability.

We urge you to resist current advocacy efforts demanding a ban on gene drive research or on the future use of gene drive-based products. Imposing a moratorium on such promising life-saving and life-improving innovations so early in their development would be unwarranted, damaging and irresponsible. Blanket bans discourage research and prevent regulators, policy-makers and other stakeholders from having an informed conversation about the use of new technologies.



Target Malaria's response to the IAS Recommendations in 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values'

Target Malaria is seeking to develop an innovative tool for vector control to help put an end to the burden of malaria in Africa. The project is researching the use of gene drive technology to reduce the population of mosquitos carrying an epidemic to levels sufficiently low to interrupt transmission. We recognise that the application of gene drive technology has tremendous potential, but also raises questions that need to be addressed comprehensively and thoroughly before any gene drive-based product can be considered for use.

Target Malaria welcomes the guidance and considerations offered by the US National Academy of Sciences in its report 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values'. Several of the recommendations highlighted by the report are already being implemented by Target Malaria. In order to advance responsible gene drive research, the project has undertaken to examine how it meets the recommendations and, where gaps exist, outline how it can improve its practices. We expect to be able to update this response as the project progresses.

5. Phased Testing and Scientific Approaches to Reducing Potential Harms of Gene Drives

5-1: Scientists conducting research on gene drives should follow a phased testing pathway, a step-by-step framework that begins with developing a research plan and continues through, if applicable, maintaining gene-drive modified organisms in the environment. Each phase in such a pathway should include pre-defined "go/no-go" decisions for determining whether to transition to the next phase based on evidence regarding harms and benefits, efficacy, and safety.

Target Malaria has adopted a staged approach for its research and development, gradually moving from genetically modified sterile male *An. gambiae* (that are not gene drive-based) through to a self-replicating modified *An. gambiae* based on gene drive. In each phase, the mosquitoes go through several steps for testing for both safety and efficacy.

Currently, Target Malaria teams are designing a number of gene drive constructs for population suppression of *An. gambiae*, and testing them in the lab in single crosses and small cages for learning about and detecting (e.g. fertility) effects. We are also currently designing additional assays for resistance and off-target effects.



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Recommendations

What can be learned...

- It's never too early to start engaging
- Important to focus primarily on those who can be affected (positively or negatively) by the research
- Importance to identify and analyse well stakeholders before starting the engagement
- Need to find the right balance between scientific precision and meaningful/understandable information and to be consistent
- Ensure it's a real engagement, not a one-way discussion
- Engage scientists in the team about the importance of engagement and potential need to reconsider plans accordingly

Acknowledgments: 14 Institutions, over 140 experts and many communities and stakeholders



Acknowledgements

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