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Gene drive for malaria vector control – from lab to application

Abdoulaye Diabate,
Institut de Recherche en Sciences de la Sante,
Burkina Faso
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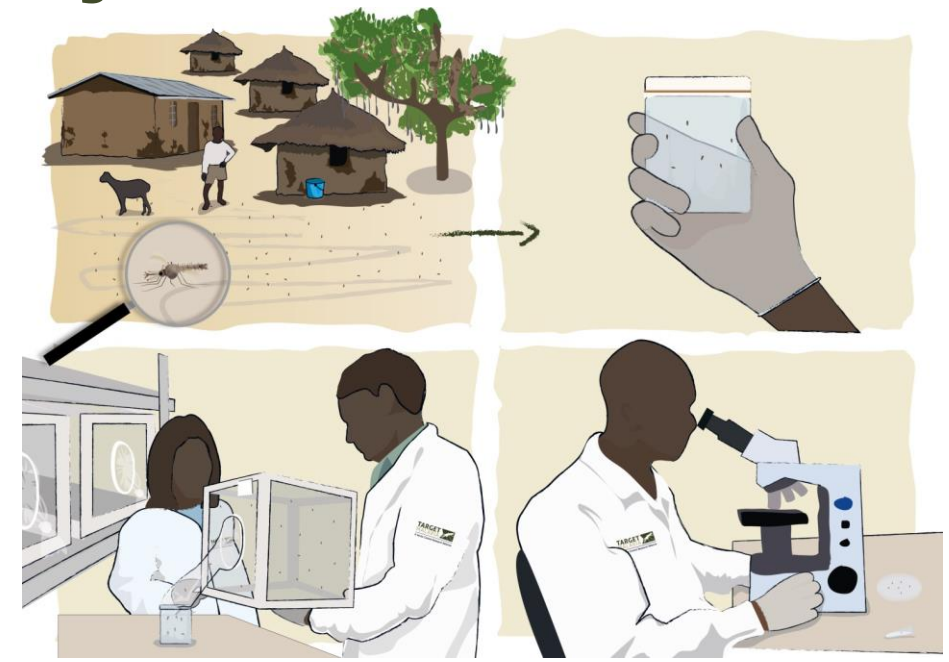
Why Malaria?



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African Experts

Dr Abdoulaye Diabate
IRSS Bobo Dioulasso

Dr Mamadou Coulibaly
MRTC Bamako

Dr Jonathan Kayondo
UVRI Entebbe

Dr Fred Aboagye-Antwi
University of Ghana Accra

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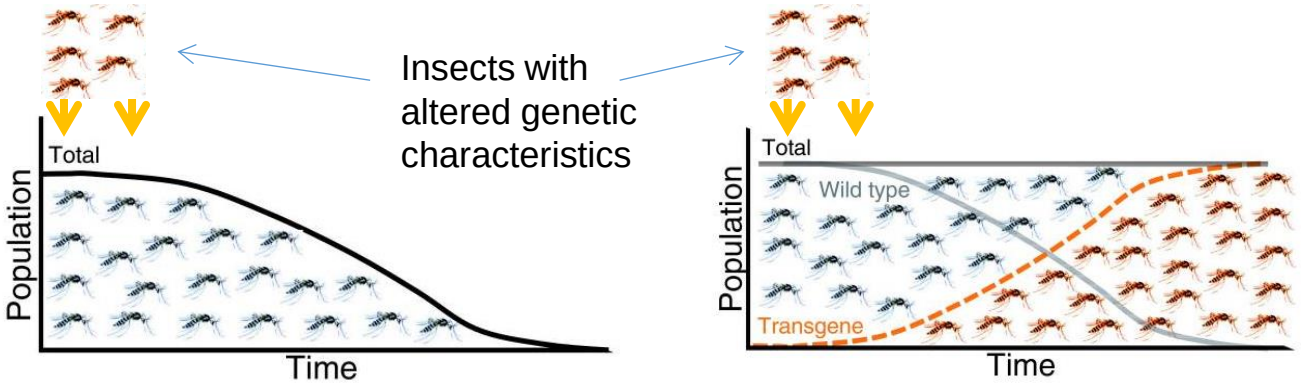
Using Insects To Do The Work - Genetic Control



Population suppression
Elimination or reduction of a wild vector population

Population replacement
Replace a pathogen-susceptible vector population with pathogen-resistant insects

Released insects do the hard job of finding difficult to reach insect niches

Species-specific

Non-toxic

Suppression and replacement strategies can be combined

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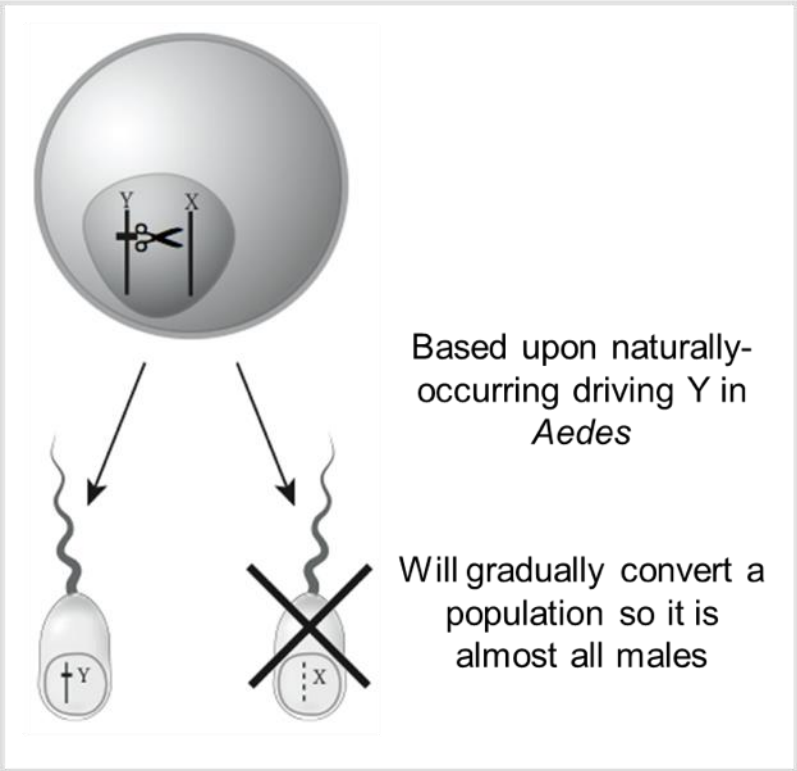
Two strategies of using nucleases

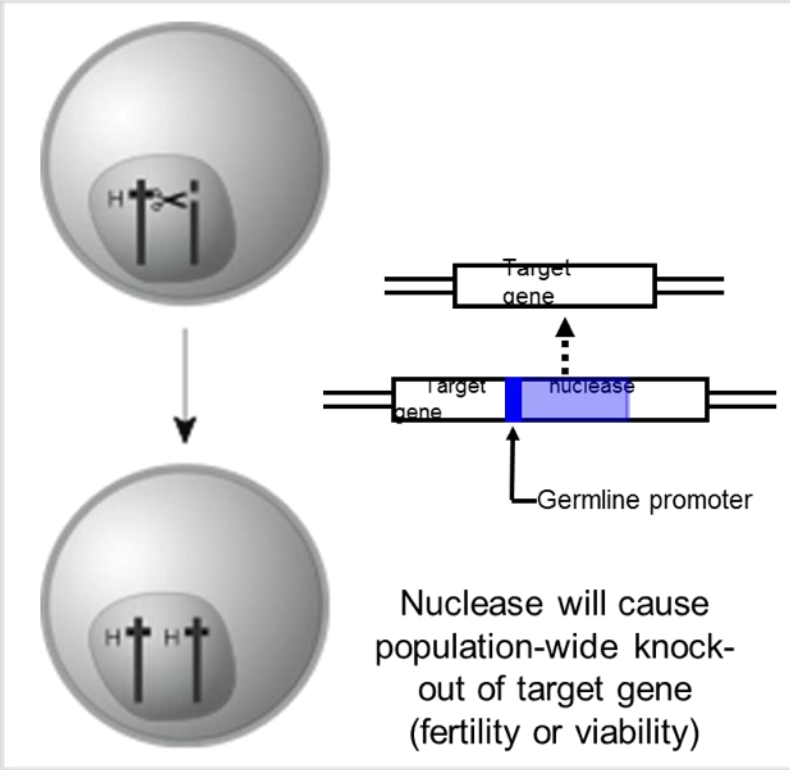
Driving Y chromosome



Based upon naturally-occurring driving Y in *Aedes*

Will gradually convert a population so it is almost all males

Gene knock-out by homing



Nuclease will cause population-wide knock-out of target gene (fertility or viability)

Both approach can suppress mosquito population

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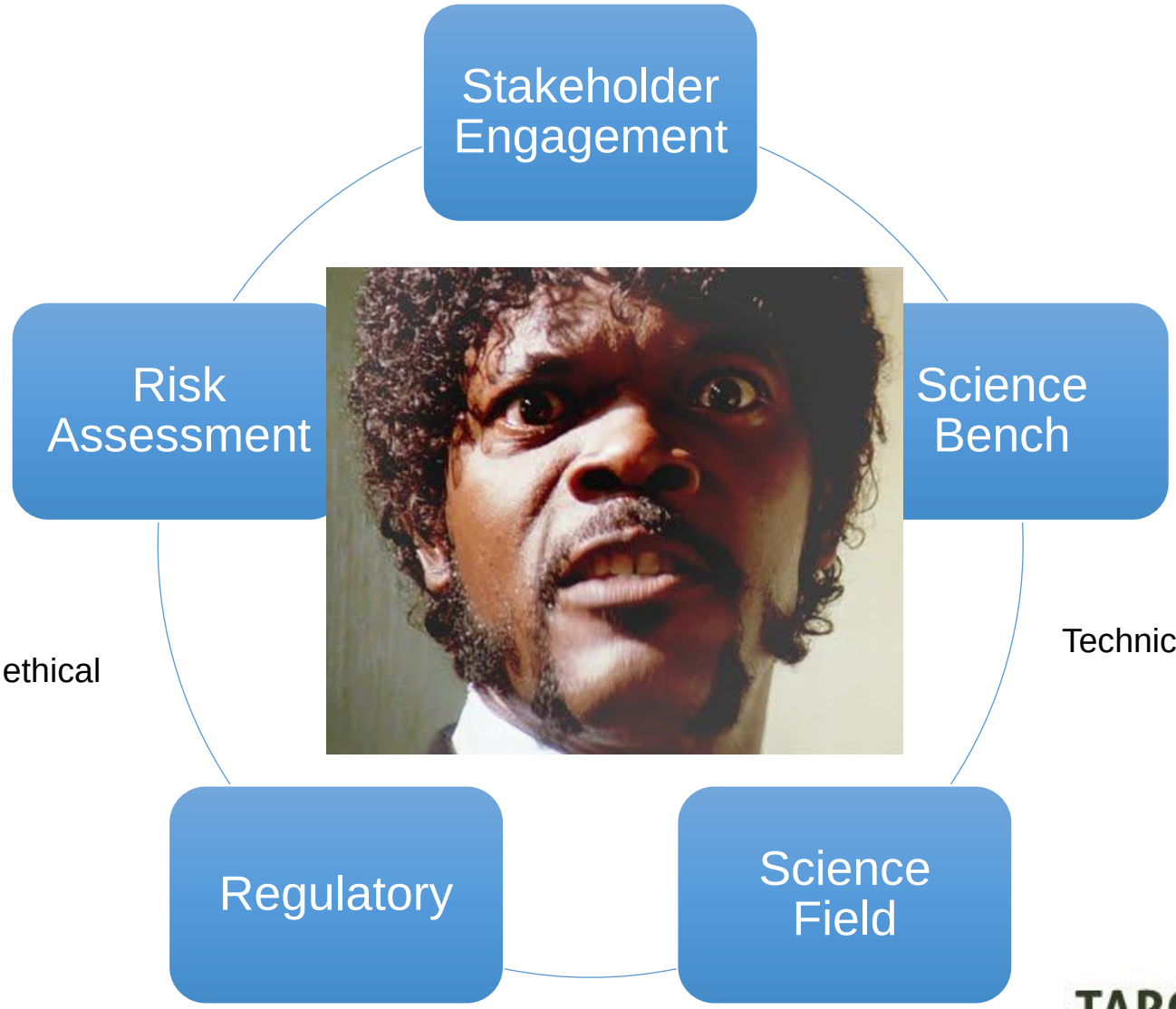
Gene drive testing hurdles



Technical challenges

Legal and ethical issues

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Safety Issues

« Safety deficiency is the one aspect that might not be easily remedied. One can gather more baseline data, one can lobby for political support and build capacity etc. but if we cannot provide a plan that people consider safe, the effort is really dead ».

Mark Benedict

Consequences of the release of gene-drive should be ascertained on a case by case basis (WHO 2014)

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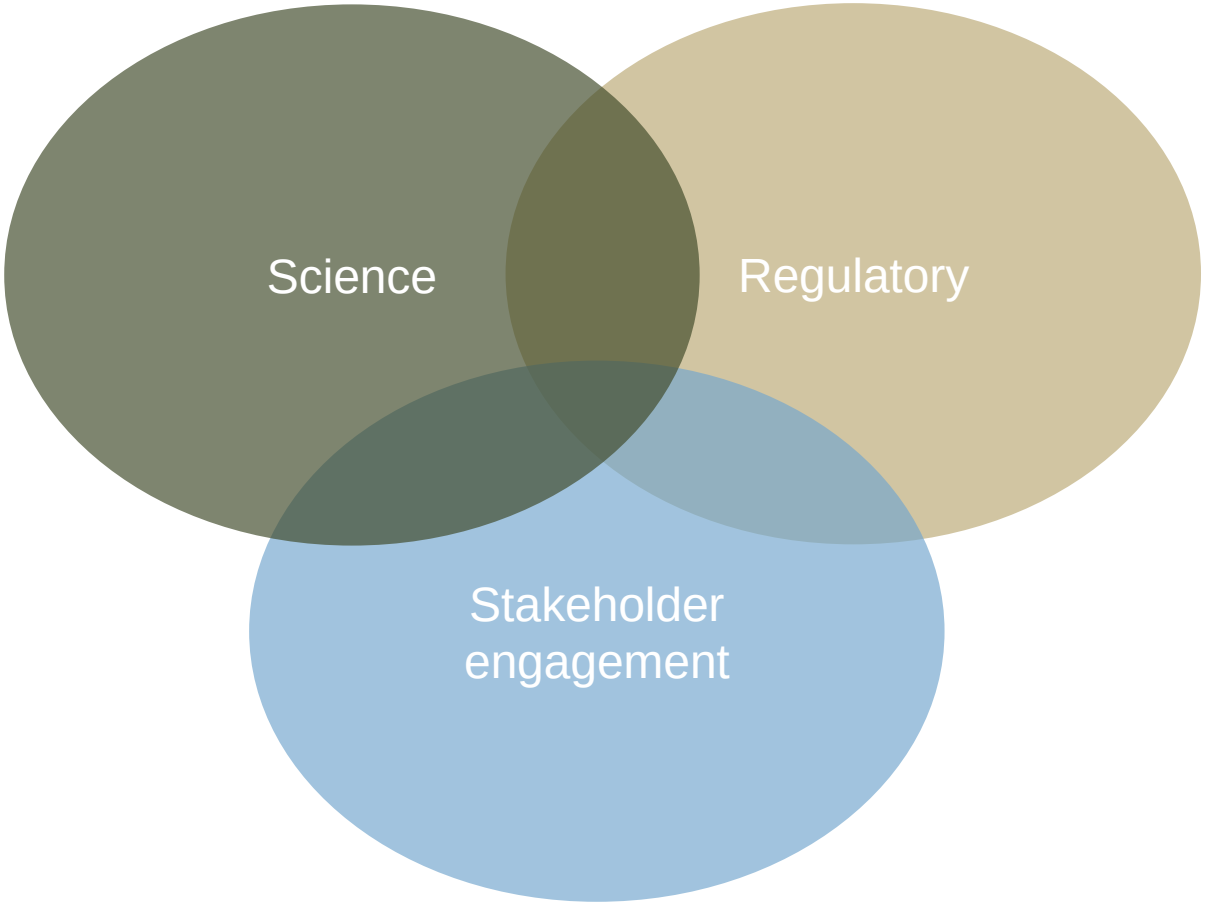
Built on three pillars



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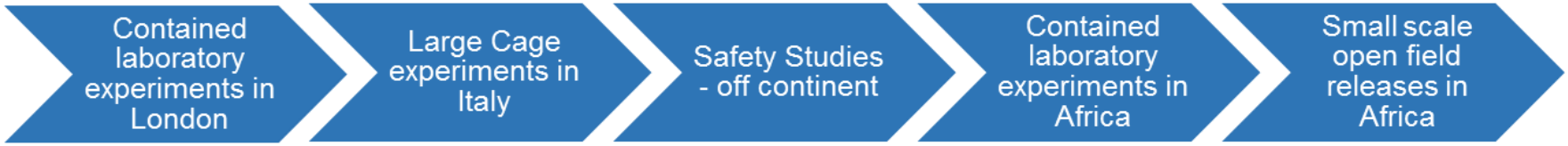
Pathway for testing each phase

- Genetically modified
- NO gene drive
- Learning phase
- No impact on malaria mosquito numbers

- Genetically modified
- Only persists for a few generations
- NO gene drive
- Currently only available for the male bias option

- Genetically modified
- With drive
- Potential long-term and sustainable impact on malaria-mosquito numbers



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Insectary readiness: Toward GMM importation

Burkina Faso

Personnel and Physical containment → **Risk Management** → **Staff training** → **SOPs and code of conduct** → **Regulation**

First project internal audit
17-25 April 2015

Factors were measured against general lab practice, specific TM policies or SOPs, national requirements on containment facilities to the degree these are known, or international practices when other guidance is not available.

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Sterile male eggs importation

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Contained use studies in Burkina Faso

contained use studies

in country

- Establish colony and introgression into ‘local’ wildtype population (An.coluzzii = Ac(DSM)2)
- Insecticide Resistance testing
- Analysis of sexual sterility
- Life history
- Mating competitiveness

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Stakeholder Engagement Challenges

Civil society

- Burkina Faso has a very active civil society
- Constitution-modification (2014)
- Removal of the president (2014)
- Protest against military coup (2015)
    - Collapse of the military coup

Social and political landscape analysis

- Map of different group of civil society
- Determine groups leaders
- Determine intervention fields of groups
- Determine pro GMO groups
- Determine Anti GMO groups
- Analyze impacts of civil society actions in national debates

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Intentional bad Communication to create Psychosis

- Target Malaria will release Monster-Mosquitoes that will eat all the wild mosquitoes. Who is next after wild mosquitoes are all eaten?

- Target Malaria will release male mosquitoes to induce sterility in female mosquitoes. What will happen to our wives when they get bitten by these sterile mosquitoes?

- Target Malaria mosquitoes have brought Dengue to Burkina Faso. You can expect worse. How about HIV?

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This is where the real work is happening, but most likely the real troublemaker will be coming from outside

Field site

Reinforce the SE work at both level but protect your sites from an outside intoxication

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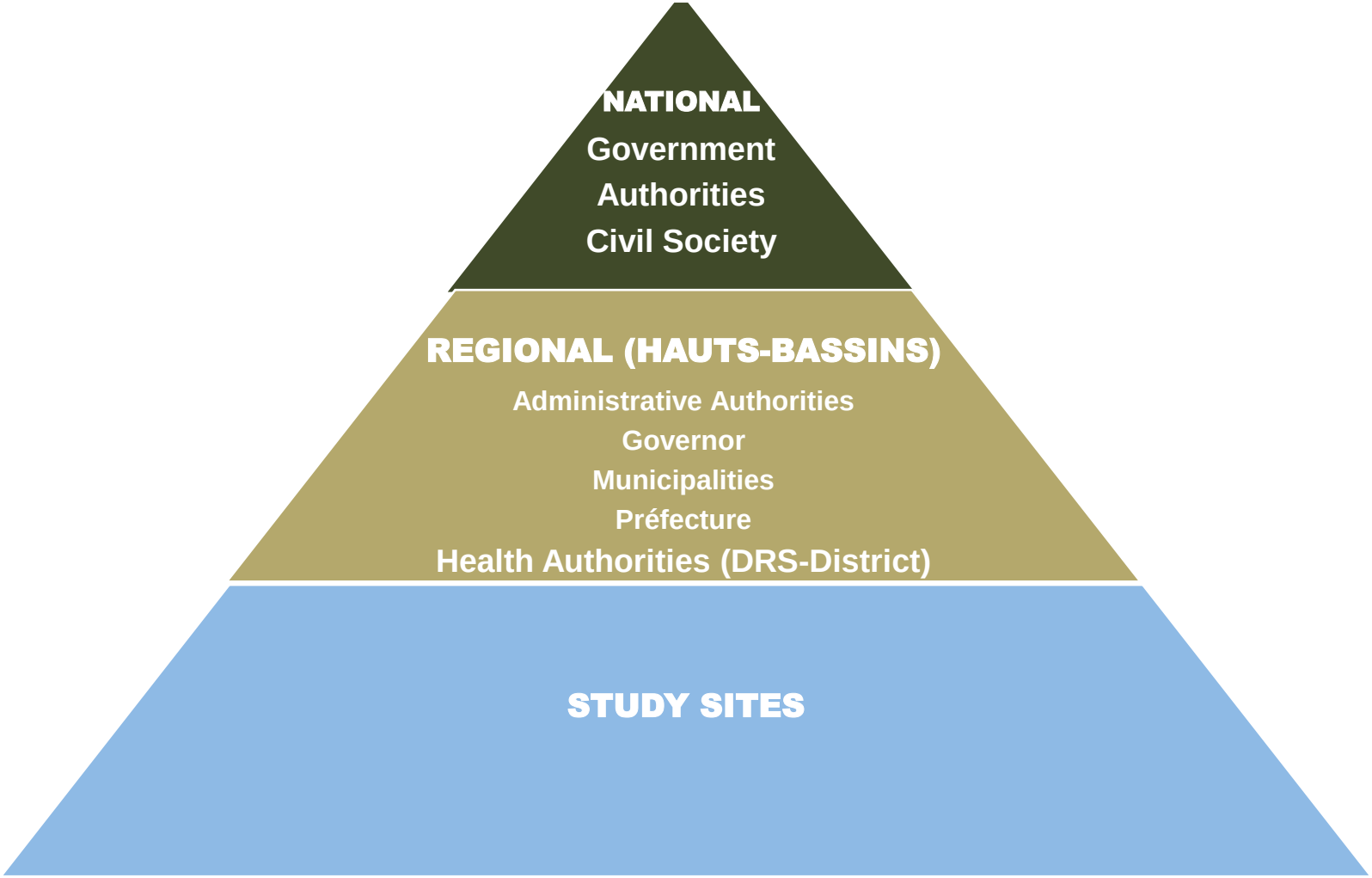
The Pyramidal Structure of Stakeholder Engagement



Stakeholder Engagement Strategy

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Ministries and Parliement

Municipalities

Peers Scientists

Traditional and Religious Authorities

Alliance

Journalists

NGOs

Villages


Dictée: l'agent recenseur.
Tous les dix ans notre pays dénombre sa population. Tôt le matin, muni de son beau sac noir, l'agent recenseur prend son vélo et s'en va vêtu d'un habit blanc avec son foulard au cou.
Malgré les intempéries et les distances, il visite toute la journée, de nombreuses habitations. Il compte le nombre de personnes de chaque ménage. Il ne revient que tard dans la soirée, tout fatigué.
Clé de correction
- Une faute entière enlève un point;
- Une demi-faute enlève 1/2 point;
Sont considérées comme une faute:
Sont considérées comme 1/2 faute:
Le point de « j » ne sera considéré.

Other studies/information for deliberate release dossier

contained use studies conducted

- Molecular characterization – single copy
- Genetic stability – 140 generations
- Mendelian inheritance confirmed
- Tissue specificity of expression –only in testes
- Bioinformatics on toxicity and allergenicity potential of introduced proteins
- Interspecific crosses

Site specific information

- Detailed information on release site
- Non-target /valued and charismatic species habitat analysis
- Stakeholder engagement and socio-economic impact assessment

Next Step: Small scale field release of sterile males

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Acknowledgements

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BILL & MELINDA GATES foundation

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