

Data Needs and Assay Design for Decision Making 2019 on Gene Drive-Modified Mosquitoes

Hyatt Regency, Newport Beach, CA

Meeting Room: Garden Room 1

Objective: To consider recommendations for:

- data required to support an application for first field testing of a new gene drive mosquito investigational product in Africa, including key predictors of entomological and epidemiological efficacy and safety for human and animal health and the environment;
- collection of relevant baseline field data;
- design of laboratory and cage efficacy and safety studies to obtain consistent data.

The focus of the workshop will be on malaria transmission by *Anopheles gambiae* in Africa.

Agenda

Monday, May 6

08:00 – 09:00 Registration and breakfast

Garden Terrace

9:00 – 9:30 Welcome and introductions – Stephanie James

9:30 – 10:15 Review of prior recommendations for measurements in Phase 1 testing

- WHO Guidance Framework for testing genetically modified mosquitoes - Mark Benedict
- Pathway to Deployment of Gene Drive Mosquitoes as a Potential Biocontrol Tool – Fredros Okumu

10:15 – 10:45 Coffee/Tea

10:30 – 11:30 Efficacy Parameters I - What to measure?

Moderator: Nikolai Windbichler

Discussion Topics:

- Life history parameters –
 - Ratio of male:female progeny
 - Males: mating competitiveness, longevity, sperm production
 - Females: fecundity, longevity after blood meal, egg hatching rate, feeding behavior
 - Development: larval-pupal development time, larval to adult survival
- Construct biology - kinetics of spread, off-target effects, inheritance bias
- Function – competence for malaria transmission (population alteration); population decline (population suppression)
- Stability of all parameters

11:30 – 12:30 Efficacy Parameters II - What to measure?

Moderator: Steve Russell

Discussion Topics:

- Resistance to effector mechanism: selection pressures from suppression mechanism, selection pressures on parasites from effector molecules

Data Needs and Assay Design for Decision Making 2019 on Gene Drive-Modified Mosquitoes

- Resistance to drive: from natural variation in gRNA target sites, from non-homologous end-joining

12:30 – 1:15 Lunch

Garden Terrace

1:15 – 2:45 How to measure?

Moderator: Greg Lanzaro

Discussion Topics:

- Influence of genetic background
 - Mosquito - how equivalent must the candidate be to wild type at the field site, what level of introgression is enough?
 - Parasite – how should lab studies take into account locally circulating strains at field site?
- Impact of dynamic conditions - temperature, humidity, density, release ratio, ...
- How long to measure - number of generations, defined endpoint?

2:45 – 3:00 Coffee/Tea

3:00 – 6:00 Translating to experimental laboratory/insectary protocols I: Design of efficacy studies

Moderators: Ken Vernick, Andrea Crisanti

Based on prior discussions, this session will consider how to design lab and cage studies to obtain efficacy data on which to base a decision to move a gene drive-modified mosquito investigational product to field testing, with a goal of identifying common approaches that will facilitate consistency and comparability of data.

6:30 – 8:30 Group Dinner

Garden Terrace

Tuesday, May 7

08:00 – 09:00 Registration and breakfast

Garden Terrace

9:00 – 10:00 Expectations for biosafety and regulatory requirements

- Anticipated requirements for regulatory dossiers - Willy Tonui
- Experiences with the regulatory process for GM mosquitoes - Abdoulaye Diabate

10:00 – 11:00 Data needs from the field

Moderator: Anton Cornel

Discussion Topics:

- Mosquito population structure and size
- Potential dispersal (active, passive)
- Interactions with other malaria control methods, including insecticide-based methods
- Insecticide resistance

Data Needs and Assay Design for Decision Making **2019** on Gene Drive-Modified Mosquitoes

- Potential for ecosystem interactions - local competitor and predator species, pollinators and other valued species

11:00 – 11:15 Coffee/Tea

11:15 – 1:00 Safety Parameters - What to measure?

Moderator: Camilla Beech

Discussion Topics:

- Vector competence – what other pathogens should be tested?
- Direct effects - toxicity, allergenicity of transgene products
- Spread of construct to other organisms – sibling species, other species
- Adverse effects on other species – predators, pollination
- Insecticide susceptibility

1:00 – 2:00 Lunch

Garden Terrace

2:00 – 5:00 Translating to experimental laboratory/insectary protocols II: Design of safety studies

Moderators: Steve Higgs, Ary Hoffmann

Based on prior discussions, this session will consider methods for lab and cage studies, and collection of baseline field data, to support risk assessment and submission of regulatory dossiers for gene drive-modified mosquitoes, including the potential for common approaches that will facilitate consistency and comparability.

(3:00 – 3:15 Coffee/tea)

5:00 – 5:30 Closing remarks - Stephanie James

5:30 Adjourn

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