Supplementary Data

SUPPLEMENTARY TABLE S1. SCIENTIFIC

Entomological data

Presence of target species (*Aedes aegypti*)

- Is the target species present at selected sites (proposed release and control sites)?
- What data are available on current and historical numbers of the target species at each location (many types of data are relevant and 'ideal' information may not be available)?
- How do those population sizes fluctuate through the different seasons of a year?
- What is the history of the target species and how have populations changed over time (again, many types of data are relevant and 'ideal' information may not be available)?

Presence of other mosquito species

- Are other mosquito species present?
- Which species appear and in what estimated or relative numbers in monitoring systems to be used (from any trapping system, but particularly from ovitraps, BG-Sentinels and backpack aspirators).

Human inhabitants

- What are the approximate numbers and demographics of the human population(s) of proposed release and control sites?

Presence of disease

- Describe the nature of dengue transmission at the proposed release trial site(s), including possible transmission by species other than *Ae. aegypti*.
- What is the history of dengue at the proposed locations? (Dengue incidence by year, season, location; is there laboratory confirmation of dengue fever and dengue hemorrhagic fever; age-specific incidence; circulating serotypes)
- What is the status of chikungunya and yellow fever viruses in the proposed sites?
- Describe the availability of facilities for monitoring dengue incidence (e.g. medical clinics, clinical research facilities) at the proposed sites, and how these are funded.
- What are the most frequent illnesses and top medical issues for people in the target community? How often are these confused with dengue fever?

Size(s) of proposed sites

- Describe the scale of site(s) in terms of geographic area (hectares or km^2). Mosquito and human populations are described in text (Entomological Data and Human inhabitants sections, respectively).

Duration of trial

- What is the capacity for commitment of the DEC partners to the duration of the trial?

Isolation

- Are the proposed sites geographically isolated by ≥ 400 meters?
- What is the nature of the isolating terrain or other barrier(s) separating the mosquito population at the site from other known or suspected mosquito populations?
- If the sites have ≤ 400 meters isolation, what mitigations are available, *e.g.*, barrier treatment in buffer zone?

Control sites

- Can a control site be identified for each potential trial site?
- To what extent are they similar and different to the proposed release sites in aspects relevant to the trial (or to what extent are there a set of comparable sites to be used either for release or as controls)?

Protected biotype and other significant resources

- Survey and describe the protected biotypes/ecotypes and other sensitive areas that are within or close to the proposed sites.

Other vector control activities

- What vector control operations are conducted in the area?
- Who is responsible for these activities?
- How are these activities funded (through which agencies/bodies of government)?
- Who are the contact people for each relevant agency?
- What is known of their program or intentions for treating (or otherwise) the proposed trial sites? Please refer to the questions in the Regulatory section about statutory or compulsory treatment.

Adverse natural conditions

- Describe the proposed site environment in terms of risk of adverse natural conditions. As appropriate, this should include locations containing laboratory facilities, access routes *etc*., as well as the proposed release sites themselves.

Adverse human activities

- What is the distance to roads, railroads, airports and other possible means by which released mosquitoes can be transmitted by humans out of the trial sites?
- Is there a real threat of civil unrest, nationally or in proposed trial area(s)?

Next steps

- If the planned trial is successful, what are the prospects for moving to a larger scale at the same or nearby site?

SUPPLEMENTARY TABLE S2. REGULATORY REQUIREMENTS

Genetically engineered mosquitoes

Legislation and permitting

- Are regulations/legislation in place governing research and other activities with recombinant DNA, etc.?
  - If so, what are the key relevant regulations/legislation?
- What is the status of the Cartagena Protocol on Biosafety (http://bch.cbd.int/protocol/) in the country and how is it being implemented?
  - If relevant, identify the in-country CPB contact point.
- Were any relevant legislation or policies in place prior to Cartagena obligations and what is their current status?
- Are there any specific laws/norms/guidance, etc., regarding vector control where project activities (*e.g.*, baseline monitoring/surveying) might interact with these regulations?
  - Any conventional control plans (*e.g.*, IVM, barrier treatment, risk mitigation plans) will need to take account of any such regulations.
- Are there other known regulatory/legal issues that may affect project operations? Examples may include:
  - Restrictive customs regulations or delays,
  - Immigration (visas, work permits),
  - Restrictions on exporting samples (for example, biodiversity/bioprospecting law).

Regulatory processes

- Has the country had previous experience importing GE mosquitoes for laboratory research?
  - If not, what about other GE insects (*e.g., Drosophila* for research purposes), plants or other animals?
- What are the relevant national, state, municipal and local agencies and their specific roles?
- Is there a clear process for application and approval for the proposed research?
  - If so, provide an outline of the structure and process.
  - What are the estimated time-lines for completing each of the regulatory steps?
  - What is the basis for this estimate?
- Is a risk assessment/risk management plan required? If so, who develops it, the applicant or the authority?
- What are the opportunities/mechanisms/requirements for public engagement in the regulatory process?
  - Some regulatory processes are fully confidential, some open to the public, some are a mix (for example, applications become publicly available but information identified as confidential by the applicant is redacted).
- What are the inspection and audit regimens for compliance with granted permits?
  - These may be described in the legislation, but in some instances may not be known in advance of the permit being granted, for example, they may be attached as conditions of permits.
- What are the internal approval procedures of the proposed in-country collaborating institution?
  - Are there precedents for prior use of these procedures?
  - What committees/structures are involved?
  - Is this a public or confidential process?
  - Are there interactions with governmental approval/permitting processes? With ethical, social, and cultural?
  - Is there sufficient capacity for regulatory compliance and reporting?

Other regulated research

- Describe the Institutional Review Boards (IRBs)/Institutional Ethics Committee (IECs) responsible for oversight of Human Subjects research at the institutions to be involved in the trials.
- Describe the Institutional Biosafety Committees (IBC) or equivalent review bodies responsible for oversight of research involving biohazardous agents.
- Describe the Institutional Animal Care and Use Committee (IACUC) or equivalent institutional review bodies responsible for oversight of research involving vertebrate animals.
- Does the country have national guidelines for research with recombinant DNA?
- Does the in-country collaborating institution have an established research review procedure for research with recombinant DNA?
  - If so, what are the procedures, structures, informational requirements and projected timescale(s)?

SUPPLEMENTARY TABLE S3. COMMUNITY ENGAGEMENT (ETHICAL, CULTURAL, AND SOCIAL)

Communication

Residents

- What are the mechanisms and conditions to facilitate interface with the trial-site residents and basis for ethical, cultural, and social (ESC) collaborations?
  - Describe any previous interactions of the collaborators with the community at the proposed trial site.
  - Is there an ongoing relationship of trust with the public health agencies and institutional scientists?
  - Describe proposed methods for informing and involving the community in preparation for trials. How would community opinions influence planning for the trials?
  - Is there any precedent or other evidence for the likely effectiveness of these methods?
- How is community engagement for vector control normally conducted in the country?
  - What is the level of understanding by communities in the proposed trial sites regarding dengue and the role of mosquitoes in transmitting dengue?
  - What process is used by public health authorities for informing the community about vector control activities? Is a mechanism for community feedback in place?

Communication Plan

- A Communications Plan will need to be put into place for both proactive and reactive communications.
  - Have stakeholders/influencers in the country and local area been identified?
  - Has a Communications Plan been developed or is one in the process of being developed?
    - At early stages this may be only in draft, outline or partial form.
- What is the local working language?
  - Do the in-country collaborators speak this language or dialect? Visiting scientists?
  - Is translation available as necessary?

Working environment

Political environment

- **What is the political system in the country/location? Relevant issues may include:**
  - Levels of government (*e.g.,* federal/state/municipal)
    - Is there conflict between levels of government likely to impose difficulties?
  - Is the political system relatively stable?
    - Are there imminent elections that may disrupt civil service (*e.g.,* collaborators or regulators), or lead to significant shifts in policy (*e.g.,* on GE organisms)?
  - If the country/site has an electoral process, when is the next election that could have a relevant impact on the proposed studies?
  - Who are the relevant authorities in the proposed field site? What are their mandates (may include health/environmental authorities, general government, etc.)?
  - Describe the cultural leadership structure of the community (are there village chiefs, groups of elders, respected religious figures and other nongovernmental figures of respect and authority?).
- Is there a political will to embrace new solutions for dengue control?
  - Evidence?
- What is the political/community history with introductions of GE organisms in the country?
  - What is the level of understanding by communities in the proposed trial-site region regarding genetic engineering?
  - Have there been previous interactions with non-governmental agency or advocacy group?
    - Components may include an overall plan/posture, key messages, frequently asked questions (FAQ) and other question and answer documents, and include local opinion leaders and third-party spokespersons.

ESC considerations

- If relevant, who has property rights at the proposed field-site location(s)?
  - Is there any risk that the research would displace individuals or communities at the preferred site(s)?
  - Is the proposed site located near to valued community resources or sites where vulnerable populations might be impacted by the trials (*e.g*., hospitals, recreational areas, schools)?

SUPPLEMENTARY TABLE S4. RESOURCES

People and institutions

- What are the reasons for interest in an open-release trial?
- What are the expectations of the collaborators?
- Provide the identity and nature of the proposed in-country collaborator and collaborating institution(s)?
  - Institution type (for example, government/university/private sector), size, identity and mission.
  - Previous history of international collaboration? With other project members?
  - Identify key individuals, for example the Principal Investigator, institute director, regulatory officer (if known)
    - Provide the background and relevant experience of key personnel.
    - What are their other duties, and how does this affect the time they have available for project?
  - As applicable, identify skill sets, gaps and training needs
  - Are there any known or foreseeable circumstances under which the institution or individuals might not be able to continue to collaborate for the full duration of project (*e.g.*, short-term contracts, institution reorganizing, unstable mission/activities/funding)

Financial/employment

- What policies govern recruitment, hiring, human resources management issues (practices and accountability) in the collaborating institution?
- What are the relative costs of operating in the country/region?
  - Cost-of-living (*e.g.*, relative to the United States or United Kingdom).
  - Indicate typical salaries for different grades (for example, graduate students, technicians, postdoctoral fellows, principle investigator other project personnel).
  - Are travel costs (flight, subsistence) and times unusually high or low?
- Any known additional costs
  - Compulsory benefits, bonuses or insurance, other employment law?
  - Regulatory costs ('user pays') and time?
  - Value Added Taxes (VAT)?

Logistics

- How far in distance is it from the collaborator's facility to the proposed field site(s)?
  - Journey time, cost, transport resources
  - Is there safe, reliable access to proposed facilities (*e.g.*, laboratories, field site and travel to/between them)? (see article sections regarding adverse natural and adverse human conditions).

Collaborator resources

- What resources does the in-country collaborator propose to provide to the project?
  - Of these, what will be funded by the collaborator, what from third-party sources and what will need to be provided from the project? Project contribution likely will be a mix of in cash and in kind, *e.g.*, provision of personnel, etc.
  - What capacity will be made available to the project to handle regulatory issues (permitting, inspections and compliance); for example, will the collaborating institutions provide people and expertise to oversee applications through the committees?
  - What is the previous experience and evidence of this?
  - What is the capacity to manage epidemiological surveillance and treatment of dengue and dengue hemorrhagic fever?
- What are the co-sponsorship opportunities?
  - Private foundations
  - Government grants
  - Resource-sharing with current vector control efforts
  - Who is eligible for applying and administering these opportunities?