AMENDED AND RESTATED INVESTIGATION AGREEMENT

This Amended and Restated Investigation Agreement (the "**Agreement**") is made on 18 August 2020 by and between OXITEC LIMITED (Company number 4512301) whose registered office is at 71 Innovation Drive, Milton Park, Abingdon, OX14 4RQ, United Kingdom ("**Oxitec**") and FLORIDA KEYS MOSQUITO CONTROL DISTRICT, a special taxing district of the state of Florida, having its principal office at 503 107th Street Gulf, Marathon, FL, 33050, United States of America ("**FKMCD**"). Each may be referred to herein as a "Party" and collectively as the "Parties."

BACKGROUND

(A) Oxitec has developed proprietary technology known as self-limiting gene technology and has created a genetically engineered (GE) strain of *Aedes aegypti* that is known as OX5034 and which is intended to be used to control wild mosquitoes of the same species (the "**Oxitec Technology**").

(B) The purpose of the Investigation (defined below) is to evaluate the effectiveness of the Oxitec Technology to reduce the local *Aedes aegypti* mosquito population in Monroe County, Florida, USA, but excluding the Key Haven community. Oxitec is the sponsor of the Investigation and is responsible for its overall management.

(C) FKMCD is interested to see the Oxitec Technology progress towards being available commercially and has therefore agreed to cooperate with Oxitec and the Investigation in accordance with and on the terms set out in this Amended and Restated Agreement.

(D) FKMCD and Oxitec had entered into a conditional Investigation Agreement on November 13, 2016 (the "2016 Investigation Agreement") to conduct an investigation upon Regulatory Clearance for Investigation al Use of the Oxitec Technology.

(E) Regulatory Authority for OX5034 sits with the Environmental Protection Agency (EPA) and an application for an Experimental Use Permit was submitted by Oxitec on March 11, 2019.

(F) This Amended and Restated Agreement revises the conditional 2016 Investigation Agreement to reflect the change in control of the Regulatory Authority and substitution of the Protocol which was submitted to the EPA for that which had been submitted to the FDA-CVM.

THE PARTIES HEREBY AGREE AS FOLLOWS:

1. DEFINITIONS

1.1 In this Agreement the following words shall have the following meanings:

Agreement	This Investigation Agreement
CDC	The Center for Disease Control of the United States of America.
Claims	All demands, claims, and liability (whether criminal or civil, in contract, tort, or otherwise) for losses, damages, legal costs, and other expenses of any nature whatsoever and all costs and expenses (including legal costs) incurred in connection therewith.
Commencement Date	The date this Agreement is executed by both Parties.
Confidential Information	All information, including technical, scientific, and commercial information, provided by Oxitec to the Recipient or to which the Recipient has access as a result of this Agreement, but only if such information operates as an exception to Florida Statutes Chapter 119 pursuant to Florida Statutes Chapters 812, 815, and other such Florida or Federal laws, that: (a) in respect of information provided in documentary or by way of a model or in other tangible form, at the time of provision is marked or otherwise designated to show expressly or by implication that it is imparted in confidence; and (b) in respect of information that is imparted orally, any information that Oxitec or its representatives informed the Recipient at the time the disclosure was imparted in confidence; and (c) any copy of any of the foregoing.
Equipment	Equipment for use in connection with the Investigation as detailed in Schedule 2.
FDACS	The Florida Department of Agriculture and Consumer Services.
Indemnified Parties	The directors, officers, employees, agents and representatives of Oxitec or FKMCD as the context requires and Oxitec's licensors.

Insectary	A secure, lockable space of at least 30 square meters provided by FKMCD on the upper floor of its Marathon office for use by Oxitec as an ACL2 (Arthropod Containment Level 2) laboratory for producing and holding the Oxitec Technology. Access to the space shall be controlled to ensure Oxitec is able to protect the fidelity of the space and those having access to the space.
Intellectual Property	Algorithms, apparatuses, databases, data collections, development tools, diagrams, formulae, inventions (whether or not patentable), know-how, trade secrets, logos, trademarks (including brand names, product names, service marks, logos, and slogans), methods, network configurations and architectures, processes, proprietary information, protocols, schematics, specifications, software, software code (in any form, including source code and executable or object code), subroutines, techniques, user interfaces, URLs, domain names, web sites, works of authorship and other forms of technology (whether or not embodied in any tangible form and including all tangible embodiments of the foregoing, such as instruction manuals, laboratory notebooks, prototypes, samples, studies and summaries), expertise and other technology applicable to formulations, compositions, products or libraries or to their manufacture, development, registration, use or marketing or to methods of testing them or processes for their manufacture, formulations containing them or compositions incorporating or comprising them, and including all biological, chemical, biochemical, toxicological, physical and analytical, safety, quality control and manufacturing data, regulatory data and filings, instructions, processes, formulae, expertise and information.
Investigation	The investigation comprises both: (a) The testing and evaluation of the Oxitec Technology by Oxitec as described in the Protocol and (b) The work set out in the Work Plan.
Losses	All losses, including financial losses, damages, legal costs and other expenses of any nature whatsoever.

Materials	The biological materials and associated information and documentation to be supplied by Oxitec under this Agreement including the Oxitec Technology together with know-how and Confidential Information relating to the Oxitec Technology as detailed in Schedule 3.
Monitoring Laboratory	A secure, lockable space of at least 15 square meters provided by FKMCD on the ground floor of its Marathon office for use by Oxitec as an ACL2 (Arthropod Containment Level 2) laboratory for evaluating field samples in accordance with the Protocol. Access to the space shall be controlled to ensure Oxitec is able to protect the fidelity of the space and those accessing the space.
Oxitec Technology	A genetically engineered strain of *Aedes aegypti* referred to as OX5034 with repressible lethality (known as self-limiting gene technology).
Project Manager	An employee of Oxitec appointed to manage the Investigation. The Project Manager will initially be Zoe Barnes.
Protocol	The protocol set out in Schedule 1 as submitted to the EPA and as amended from time to time by agreement with the EPA (where required).
Results	All data generated as a result of the Investigation.
Regulatory Clearance	Notification from the EPA and FDACS that it does not object to the Investigation being undertaken and/or notification from the EPA and FDACS that it does not object to the Oxitec Technology being marketed as the context requires.
Secondee	A suitably qualified employee of FKMCD designated to work as part of the Project Team under the oversight of the Project Manager for the duration of the Investigation. For the avoidance of doubt the Secondee will at all times remain an employee of FKMCD and Oxitec shall not at any point in time or under any circumstances be regarded as the employer of the Secondee but the Secondee will report to the Project Manager for the duration of the Investigation insofar as the Secondee is assisting in Project Team Duties and not performing regular FKMCD duties.

Sponsor Representative	An employee of Oxitec appointed to be responsible for the Protocol and all interactions with the regulator under this Agreement. The Sponsor Representative shall initially be Nathan Rose.
Term	The period from the Commencement Date until the completion of all aspects of the Protocol and Work Plan unless terminated earlier in accordance with clause 11. Not to exceed 22 months after initial release of mosquitoes.
Territory	The whole of the Keys area within Monroe County in the State of Florida, USA including the Upper, Middle and Lower Keys, but excluding the community of Key Haven.
Third Party	Any person other than the Parties.
USDA	United States Department of Agriculture.
Work Plan	The tasks specified in Schedule 4 and the timetable for performing them.

2. THE INVESTIGATION

2.1 The Parties agree that the Investigation shall not begin until Oxitec has:

(a) received Regulatory Clearance from the EPA and FDACS that the Investigation may be undertaken in an agreed upon location within the Territory;

(b) received necessary permits to import and deliver a shipment of the Oxitec Technology to the Insectary (which may include permits from EPA, US Fish and Wildlife Services, USDA and/ or CDC).

2.2 The Parties shall undertake and perform their respective roles in the Investigation in accordance with the Protocol and as described in this Agreement and shall ensure that all directions from the EPA, whether given at the time of Regulatory Clearance or subsequently, are followed by all those involved in the conduct of the Investigation.

2.3 Both Parties recognize the importance commercially of the Investigation to Oxitec and that the Investigation is of no value to Oxitec if it is terminated early or conducted outside of the Protocol. The Parties therefore agree to use their best efforts to ensure that the Investigation takes place strictly in accordance with the Protocol and that time shall be of the essence.

2.4 Notwithstanding the foregoing, the release of the Oxitec Technology may not commence without the consent of the FKMCD Executive Director.

3. ORGANIZATION OF THE INVESTIGATION

3.1 The Parties will establish a Steering Committee with responsibility for overseeing the management and conduct of the Investigation. The Steering Committee shall consist of three or four members designated by each Party. The initial members from Oxitec shall be Grey Frandsen, Kevin Gorman and other(s) to be confirmed. The initial members from FKMCD shall be Andrea Leal and her Designee(s). Either Party may vary its member(s) of the Steering Committee by giving written notice to the other Party. It is understood that this Steering Committee has not been granted any other decision-making authority by the Board of FKMCD and that the Steering Committee only acts to carryout operations pursuant to this Agreement as previously authorized by the Board of FKMCD.

3.2 The Steering Committee shall oversee the following proprietary decisions and/or trade secret information (excluded from the Sunshine Law by Florida Statutes section 815.045 and Florida Law):

(a) receive regular reports from the Project Manager on the progress of the Investigation including the implementation of the Work Plan, and shall monitor the conduct, nature, progress and results of the Investigation (recognizing that day-to-day monitoring of data and results from the Investigation shall be the responsibility of the Project Manager);

(b) amend the Work Plan as required and consider amendments to the Protocol as described in clause 5;

(c) allocate resources and tasks in relation to the Work Plan and the Investigation between the Parties and record such allocation in revisions to the Work Plan from time to time;

(d) meet monthly or at such intervals as it considers appropriate to undertake its obligations. Such meetings may be in person, by video or telephone conference as agreed by the Steering Committee;

(e) take into consideration the local situation concerning COVID-19 prior to commencement of releases at a date no earlier than January 1st 2021; and

(f) perform any other functions specified in this Agreement.

3.3 The meetings of the Steering Committee shall be chaired by a member of the Steering Committee employed by Oxitec. Meetings shall be convened by the chairman with at least seven (7) days prior notice, accompanied by an agenda. The agenda shall be deemed to be accepted unless one of the Steering Committee members notifies the chairman and the other members in writing, which notice may be given by e-mail, of additional points to add to the agenda at the latest two (2) days before the date of the meeting. At meetings of the Steering Committee decisions shall be made by a majority of the votes cast. Nothing in this

section or in this Agreement provides Oxitec with any rights or authority over any other District employee, business, or project other than this Investigation as stated herein.

3.4 The Parties agree that FKMCD shall retain control and authority over the quantity of resources allocated to the project. Such control and authority will be discussed with the Steering Committee for any concerns or input. While every effort will be made to accommodate the recommendations of the Steering Committee, the Parties expressly recognize that the primary mission of the FKMCD remains the abatement and control of arthropods.

(a) The Parties may establish an Independent Advisory Panel with responsibility for providing advice and guidance where sought pertaining to the Investigation. The Steering Committee will retain all decision-making authority. The Advisory panel may consist of up to five people, each to be agreed in advance by the Steering Committee. Members of the Independent Advisory Panel will execute Nondisclosure Agreements no less stringent than the obligations of confidentiality in this Agreement. The Steering Committee may disband the Independent Advisory Panel at any time.

3.5 Project Team

(a) The day-to-day implementation and management of the Work Plan and Investigation shall be carried out by the Project Team under the management of the Project Manager. The Project Team shall comprise the Project Manager, another employee of Oxitec, Secondees (as appointed by FKMCD) and any further resources that may be approved by the Steering Committee. Should the Steering Committee decide at any stage that any Secondees of FKMCD are unsuitable, FKMCD will use its best endeavors to replace them with more suitable Secondees.

(b) The functions of the Project Team shall include:

1. conducting the Investigation in accordance with the terms of the Protocol and in accordance with the law;

2. collecting and reviewing the data and results from the Investigation and compiling and agreeing to the content of reports to the Steering Committee;

3. allocating project tasks in accordance with the Work Plan and resource availability;

4. informing the Steering Committee of any disagreement among the members of the Project Team with regard to any matter requiring a decision and affecting the progress of the project in order that the Steering Committee may determine how to resolve the issue;

5. reviewing and considering whether any changes might be needed to the Work Plan or Protocol or any changes to releases specified in the Protocol and making recommendations to the Steering Committee concerning changes to the Work Plan and/or Protocol and any other matters affecting the Investigation.

(c) The Project Team shall seek to operate by consensus but the Project Manager shall allocate roles, tasks and methods and shall refer to the Steering Committee any matter requiring decision about which agreement cannot be reached within the Project Team.

4. ALLOCATION OF SPECIFIC RESPONSIBILITIES

4.1 For the purposes of obtaining Regulatory Clearance and conducting the Investigation in compliance with 40 C.F.R. § 152 Oxitec shall be the Sponsor of the Investigation and shall therefore be responsible for performing the actions specified in 40 C.F.R. §152.

4.2 FKMCD shall be identified as the U.S. legal entity responsible for the importation of the Oxitec Technology on the import and movement permit application forms and employee(s) or agent(s) of Oxitec shall be nominated as the authorized user(s). The Parties shall collaborate to obtain and comply with these permits.

4.3 FKMCD shall:

(a) Assist Oxitec in carrying out diligently the work detailed in the Protocol in accordance with the provisions of the Protocol and accompanying Standard Operating Procedures (SOPs) with the highest current scientific and technological standards;

(b) Provide suitably qualified personnel to assist Oxitec with the Investigation as Secondees to work as part of the Project Team;

(c) Provide Oxitec unrestricted access to the Insectary for the purposes of producing and holding the Oxitec Technology;

(d) Provide Oxitec unrestricted access to the Monitoring Laboratory for the purposes of analyzing field samples;

(e) Provide the Equipment listed in Schedule 2 to the Project Team to conduct the Investigation in accordance with the Protocol;

4.4 FKMCD shall use its best endeavors to ensure that all work carried out under this Agreement by it or by any of its employees, officers, agents or representatives complies with all relevant laws, regulations, practices, operating procedures, codes, and all relevant guidelines, including without limitation legislation appropriate to pesticide investigations, the processing of data and the requirements of the EPA and FDACS.

4.5 Apart from the analysis required by the Protocol, or requested by Oxitec, FKMCD shall not carry out or permit any Third Party to carry out any other studies relating to unpublished Results or data or samples arising from or taken in the course of the Investigation without the prior written agreement of Oxitec. Notwithstanding the foregoing, the Parties recognize that no such prohibition exists for public engagement survey studies.

4.6 Each Party shall perform its obligations in connection with the Investigation including all steps taken to obtain Regulatory Clearance for the Investigation at its own expense and in accordance with all applicable laws, regulations, industry norms and standards.

4.7 The Parties acknowledge that the regulations applicable to the Investigation will be those for pesticide registration under the EPA. The Parties agree to work closely together, to be flexible and to cooperate fully with one another to accommodate any changes in the regulatory environment in accordance with both the spirit and the letter of this Agreement. To that end FKMCD shall disclose all Investigation data to Oxitec in relation to any application Oxitec may make for authorization, approval or clearance in connection with the use of the Oxitec Technology on a commercial basis based on the Investigation results.

4.8 FKMCD and Oxitec recognize and agree to comply with all applicable provisions of Florida Statutes Chapter 119 (as may be amended from time to time) and all other laws, rules and regulations regarding the need to keep public records and provide the public with access to those records.

4.9 The Parties recognize the majority of Oxitec's activities will not involve Oxitec acting on behalf of the FKMCD and thus should not be subject to Florida Chapter 119. However FKMCD must and will comply with all Public Records and Sunshine laws in handling of documents, including any documentation that is provided to FKMCD unless such documentation is exempt or confidential and exempt from public records disclosure requirements. Oxitec agrees to comply with Florida Statute § 119.0701, insofar as such section is applicable to Oxitec, set forth herein, as may be amended from time to time, and understands its duties and requirements under § 119.0701(b)(1-4), which states as follows:

(1) Definitions. - For purposes of this section, the term:

(a) "Contractor" means an individual, partnership, corporation, or business entity that enters into a contract for services with a public agency and is acting on behalf of the public agency as provided under s. 119.011(2).

(b) "Public agency" means a state, county, district, authority, or municipal officer, or department, division, board, bureau, commission, or other separate unit of government created or established by law.

(2) Contract requirements.- In addition to other contract requirements provided by law, each public agency contract for services entered into or amended on or after July 1, 2016, must include:

(a) The following statement, in substantially the following form, identifying the contact information of the public agency's custodian of public records in at least 14-point boldfaced type:

If the contractor has questions regarding the application of Chapter 119, Florida Statutes, to the Contractor's duty to provide public records relating to this contract, contact the Custodian of Public

Records at (telephone number, e-mail address, and mailing address).

(b) A provision that requires the contractor to comply with public records laws, specifically to:

(1) Keep and maintain public records required by the public agency to perform the service.

(2) Upon request from the public agency's custodian of public records, provide the public agency with a copy of the requested records or allow the records to be inspected or copied within a reasonable time at a cost that does not exceed the cost provided in this chapter or as otherwise provided by law.

(3) Ensure that public records that are exempt or confidential and exempt from public records disclosure requirements are not disclosed except as authorized by law for the duration of the contract term and following completion of the contract if the contractor does not transfer the records to the public agency.

(4) Upon completion of the contract, transfer, at no cost, to the public agency all public records in possession of the contractor or keep and maintain public records required by the public agency to perform the service. If the contractor transfers all public records to the public agency upon completion of the contract, the contractor shall destroy any duplicate public records that are exempt or confidential and exempt from public records disclosure requirements. If the contractor keeps and maintains public records upon the completion of the contract, the contractor shall meet all applicable requirements for retaining public records. All records stored electronically must be provided to the public agency, upon request from the public agency's custodian of public records, in a format that is compatible with the information technology systems of the public agency.

4.10 **IF THE CONTRACTOR HAS QUESTIONS REGARDING THE APPLICATION OF CHAPTER 119, FLORIDA STATUTES, TO THE CONTRACTOR'S DUTY TO PROVIDE PUBLIC RECORDS RELATING TO THIS CONTRACT, CONTACT THE CUSTODIAN OF PUBLIC RECORDS AT 305-292-7190, email: cbloxom@keysmosquito.org, 503 107th Street Gulf, Marathon, Florida, 33050.**

4.11 Oxitec shall defend and indemnify FKMCD as to any disagreement, disputes, claims, or lawsuits regarding the retention or release of public records by Oxitec, including, if applicable, Florida Statutes Chapter 119 and the Sunshine law.

5. AMENDMENT OF THE PROTOCOL

5.1 The Protocol shall be amended solely by the Sponsor Representative, who shall communicate such amendments in writing to the EPA.

5.2 Before making any material amendment to the Protocol (as that term is defined in the Protocol), including to the Protocol's Standard Operating Procedures, Oxitec will make reasonable efforts to present the amendment and its rationale to the Steering Committee to permit discussion before finalizing the amendment. The Sponsor Representative will notify in writing (including by email) the Project Manager and all members of the Steering Committee of all amendments, whether or not material and whether or not discussed by the Steering Committee, within 3 working days of the amendment being made.

5.3 If FKMCD is dissatisfied with or would like to change any aspect of the Protocol, it will raise the concern and/or any proposed amendment with the Steering Committee.

5.4 Any amendment shall be deemed to be incorporated into the Protocol and/or Standard Operating Procedures only after the Sponsor Representative notifies the Project Manager as provided in this Section 5.

6. USE OF THE MATERIALS

6.1 Oxitec shall be responsible for maintaining the Materials within the Insectary, for transporting the Oxitec Technology to the field and releasing it there, and for transporting field samples to the Monitoring Laboratory, all in accordance with the Protocol.

6.2 FKMCD shall:

(a) use the Oxitec Technology and the Equipment only in accordance with the Protocol, and as directed by the Project Manager and shall comply with all reasonable instructions given by Oxitec and/or its Project Manager from time to time in relation to the use of the Materials;

(b) not provide the Oxitec Technology or the Equipment to any Third Party except as contemplated in this Agreement or required by law;

(c) not perform any compositional, structural or other analysis of the Oxitec Technology, the Materials or the Equipment or undertake any reverse engineering in relation to the Oxitec Technology, the Materials or the Equipment, without Oxitec's prior written consent;

(d) not remove the Oxitec Technology from the Insectary nor provide access to the Insectary or the Monitoring Laboratory to any employee of FKMCD or to Third Party without the prior written authorization of Oxitec or the Project Manager;

(e) nothing in this clause 6.2 prevents FKMCD permitting access to the Insectary or Monitoring Laboratory without prior written authorization in emergency circumstances or in circumstances where preventing such access would contravene legislation or as otherwise required by law and Oxitec is informed as soon as reasonably possible.

6.3 FKMCD shall ensure that all Secondees of FKMCD assigned to work with the Project Manager cooperate fully with the Project Manager during the Secondees' assigned time. The Steering Committee reserves the right to exclude individual Secondees of FKMCD from the Project Team should the Committee deem necessary.

6.4 The Equipment, Materials and any copies thereof made by or in the possession of or under the control of FKMCD pursuant to this Agreement shall at all times remain the property of Oxitec (or its licensors) and no transfer of title shall occur under the terms of this Agreement. The Equipment, Materials and any copies thereof (not including records subject to Florida Statutes Chapter 119 or Florida Statute § 119.0701 as provided above in clause 4.10 and 4.11) made by or in the possession of or under the control of FKMCD shall be immediately returned or, if Oxitec so requests, destroyed to the extent allowed by law.

6.5 Except as expressly provided by this Agreement, no license under any of Oxitec's Intellectual Property is granted or implied by this Agreement.

6.6 FKMCD understands and acknowledges that the Material incorporates the valuable Intellectual Property, know-how and Confidential Information of Oxitec and its licensors, and that Oxitec and its licensors own all such Intellectual Property rights in and to the Material. FKMCD further recognizes that nothing contained in this Agreement shall be construed as granting to FKMCD any rights to such Intellectual Property or such confidential information, or to any invention or patent right that has issued or may issue based on the Material, or anything contained therein or derived there from. Further, FKMCD shall not remove, amend, alter or obscure any notices relating to Intellectual Property on any packaging, documents or material accompanying or forming part of the Material and/or Equipment.

7. INTELLECTUAL PROPERTY & CONFIDENTIALITY OBLIGATIONS

7.1 All Results and any Intellectual Property embodied therein shall be owned exclusively by Oxitec. FKMCD hereby assigns to Oxitec all rights in and to any Intellectual Property created or arising from the Investigation for the full duration of such rights, wherever in the world enforceable. FKMCD agrees to execute all documents and assignments and do all such things as may be necessary to perfect Oxitec's title to the Intellectual Property or to register Oxitec as owner of any registerable rights to the best of FKMCD's ability. Nothing herein shall require FKMCD to defend any claimed Intellectual Property rights.

7.2 As between Oxitec and FKMCD, all Confidential Information belongs solely to Oxitec. FKMCD shall not, during the Term and for a period of five (5) years thereafter, disclose to any Third Party nor use for any purpose except the Investigation any Confidential Information.

7.3 The obligations of confidentiality and non-use set out in Clause 7.2 shall not apply to any information, whether Confidential Information or not, that FKMCD can show by way of written record:

(a) is required to be disclosed by FKMCD to comply with the applicable laws or governmental regulations provided that FKMCD, where possible, notifies Oxitec, of such requirement prior to any such disclosure, and FKMCD takes whatever steps it can to limit the disclosure of commercially sensitive information relating to or disclosed by Oxitec;

(b) was known to FKMCD before the information was imparted by Oxitec;

(c) is in or subsequently becomes publicly known through no fault, act, or omission on the part of FKMCD;

(d) is received by FKMCD without restriction on disclosure or use from a Third Party lawfully entitled to make the disclosure to FKMCD without such restrictions.

7.4 FKMCD warrants that all of its employees will be made aware of the obligations of confidentiality that it has agreed to above in connection with the Investigation and this Agreement.

8. COMMUNICATION, PUBLICATION & ANNOUNCEMENTS

8.1 Nothing in this Agreement is intended to limit comments by Board members at public meetings or when speaking in their official capacity as Commissioners of the FKMCD.

8.2 Nothing in this Agreement is intended to circumvent requirements of FKMCD under the Florida Sunshine Law, Chapters 119 and 286.

8.3 Nothing in this Agreement is intended to limit comments by FKMCD staff regarding operational and budgetary issues.

8.4 Nothing in this Agreement shall preclude any disclosure to the extent required by applicable law, rule or order of court, or government regulation. Notwithstanding the foregoing, in the event that any demand or request for disclosure of Confidential Information is made pursuant to this Section 8.4, either Party, as the case may be, shall promptly notify the other Party of the existence of such request or demand and shall provide the other Party with a reasonable opportunity to seek an appropriate protective order or other remedy, which both Parties will cooperate in seeking to obtain. In the event that such appropriate protective order or other remedy is not obtained, the Party whose Confidential Information is required to be disclosed shall or shall cause the other Party to furnish, or cause to be furnished, only that portion of the Confidential Information that is legally required to be disclosed and shall be approved by the Steering Committee.

8.5 Both Parties recognize the importance of maintaining the independent nature of the other under this Agreement. Both Parties will endeavor to work with the other, including through the Steering Committee, to maintain a consistent approach to communications with the Public and to avoid the disclosure of Oxitec's confidential information. However, should the situation require a response, or should the need arise for either Party to communicate with the public, constituents or others regarding Confidential Information covered by this

Agreement, such communication will only be disclosed subject to the approval of the Steering Committee.

9. LIABILITY

9.1 Oxitec agrees to take out and maintain for the duration of the Investigation until the termination of this Agreement in accordance with clause 11 the following insurance policies, adding FKMCD as an additional insured, to meet Third Party Claims and Losses for which Oxitec is held to be liable by a court of competent jurisdiction in respect of activities undertaken by Oxitec pursuant to the terms of this Agreement, and which shall not contain any endorsement(s) excluding nor limiting cross liability coverage:

(a) Public liability insurance to the value of five (5) million dollars (USD);

(b) Product liability insurance to the value of five (5) million dollars (USD);

(c) Pollution and contamination liability insurance to the value of three (3) million dollars (USD).

(d) Automobile insurance covering any Oxitec employee using a FKMCD vehicle as provided in Schedule 2 to the value of one (1) million dollars (USD).

9.2 Subject to the limitations as set forth in Chapter 768, Florida Statutes, each Party shall indemnify and hold harmless the other Party from all Claims and Losses arising from the failure of that Party, its employees or agents to conduct the Investigation in accordance with the Protocol and/or with clauses 6.1 and 6.2. FKMCD does not waive its right to immunity or limitations as set forth in Chapter 768, Florida Statutes.

9.3 Subject to the limitations as set forth in Chapter 768, Florida Statutes, FKMCD and Oxitec (the 'Indemnifying Party') shall each defend, indemnify and hold the other Party (the 'Indemnified Party'), including their officers and employees, harmless in addition to the Indemnified Parties from and against any and all liabilities, claims, damages, penalties, demands, judgments, actions, proceeds, losses or costs, including but not limited to reasonable attorneys' fees and paralegals' fees for which the Indemnifying Party is held liable by a court of competent jurisdiction including but not limited to Claims and Losses arising from: (a) injury to the other Party's employees, directors, officers, agents and representatives and/or Third Parties, and/or (b) the use, keeping or treatment of the Materials (for which the Indemnifying Party was responsible) outside the scope of the Protocol and/or (c) access gained to the Insectary by any Third Party without Oxitec's prior written permission and/or (d) public records claims. FKMCD does not intend to waive its right to immunity or limitations as set forth in Chapter 768, Florida Statutes nor should anything in this Agreement operate as a waiver thereof.

9.4 A Party's duty to defend the other Party under this Section 9 is independent and separate from the duty to indemnify, and the duty to defend exists regardless of any ultimate liability of Oxitec, FKMCD, and any Indemnified Party. The duty to defend arises immediately upon presentation of a claim by any Party or Third Party and written notice of such claim

being provided to the Indemnifying Party. The Indemnifying Party's obligation to indemnify and defend under this Section 9 will survive the expiration or earlier termination of this Agreement until it is determined by final judgment that an action against the Indemnified Party for the matter indemnified hereunder is fully and finally barred by the applicable statute of limitations.

9.5 FKMCD and Oxitec recognize and agree that Executive Director Andrea Leal (or her successor) shall at all times be acting and performing as the agent and servant of FKMCD and the Executive Director shall exercise exclusive control or direction over the method and manner by which Executive Director performs her services and functions on behalf of FKMCD.

9.6 Oxitec undertakes to make no claim in connection with this Agreement or its subject matter against the Executive Director and/or the FKMCD Board apart from claims based on fraud or willful misconduct.

9.7 Nothing in this Agreement shall, as between the Parties, exclude the liability of Oxitec for any loss or damage suffered by a Third Party as a direct consequence of the release of the Oxitec Technology in the Territory in accordance with the Protocol.

9.8 Nothing in this Agreement shall exclude or restrict the liability of a Party for death or personal injury caused by the negligence of that Party or for fraud, subject to the limitations of Florida Statute Chapter 768.

9.9 Neither Party shall be liable to the other for any consequential or economic loss including but not limited to loss of profit, business goodwill, turnover or any other loss arising from its performance or non-performance of its obligations in connection with this Agreement whether arising from breach of contract, tort, breach of duty, negligence or any other cause of action.

10. WARRANTIES

10.1 The Parties warrant that they shall each abide by all applicable governmental regulations and guidelines when handling and using the Material and shall ensure that all employees of either Party handling or using the Materials on behalf of either Party behalf are technically qualified to do so.

10.2 Oxitec is the owner of, applicant for and/or the registered proprietor of, a number of Intellectual Property rights (including patents) around the world relating to aspects of its self-limiting gene technology incorporated within or forming part of the Materials however Oxitec makes no warranty regarding the existence and/or validity of such rights in the USA. Oxitec agrees to indemnify, defend and hold FKMCD harmless in the event that legal action is brought or threatened against FKMCD alleging infringement of Third Party rights as a result of the use of the Materials in the Territory in accordance with the Protocol. FKMCD shall promptly provide Oxitec with full details of any such legal action or threatened legal action and the Parties shall discuss and agree the best way to respond.

FKMCD will be fully and completely indemnified and defended until final resolution of such suit.

10.3 The Materials made available by Oxitec include biological materials that are experimental in nature, and Oxitec makes no representation and gives no warranty as to the performance of the Materials in any particular manner, that they are fit for any particular purpose or that the Material will not have any latent or other defect.

11. DURATION AND TERMINATION

11.1 This Agreement, and the licenses granted hereunder, shall come into effect on the Commencement Date and, unless terminated earlier in accordance with this Clause 11, or as a result of delay or rejection by the EPA of the application for Regulatory Clearance of the Investigation or notification of a decision by the EPA that the Investigation must cease, it shall continue in force until the end of the Term, and on such date this Agreement shall terminate automatically by expiry.

11.2 The Parties may terminate this Agreement at any time by mutual written agreement signed by the authorized signatories of the Parties.

11.3 Upon termination of this Agreement for any reason (and unless otherwise agreed by the Parties in a subsequent, written agreement):

(a) FKMCD shall return to Oxitec, or at Oxitec's request, destroy any and all Equipment, Materials (including biological materials) and any documents or other materials that are in FKMCD's possession (excluding those held within the Insectary which Oxitec shall be responsible for removing and/or destroying) or under its control incorporating Confidential Information belonging to Oxitec, to the extent allowed by law, and shall within fourteen (14) days of so doing provide Oxitec with a sworn statement confirming that all Materials (including those stored electronically) have been destroyed or delivered up, as directed by Oxitec, and that it no longer has any such materials in its possession or under its control. Nothing in this clause 11.3(a) allows the deletion or destruction of any public records as defined and required by Florida Statutes Chapter 119 or Florida Statute § 119.0701 as provided above in clause 4.10 and 4.11.

(b) All rights and licenses granted by Oxitec under this Agreement shall cease to have effect.

(c) The Parties shall discuss and may agree the basis upon which Oxitec may continue to use the Insectary, Monitoring Laboratory and any Equipment provided by the FKMCD in the event they are still required by Oxitec following termination. Neither Party is under any obligation to continue to use or permit the use of the Insectary, Monitoring Laboratory and any such Equipment. Continued use and occupation of FKMCD property following termination shall be at the sole option and discretion of FKMCD.

12. DISPUTE RESOLUTION

12.1 If any dispute arises in connection with this Agreement the Parties, or representatives thereof with full settlement authority, shall physically attend and participate in mediation in good faith. Either Party may attend the mediation telephonically or via video conference with the other Party's written permission. The requirement to attend mediation in the manner set forth in this paragraph shall be a condition precedent to filing a lawsuit. The Party who seeks resolution of a controversy, claim, dispute, or other matter in question shall notify the other Party in writing of the existence and subject matter of the matter in question and shall designate in such notice the names of three prospective mediators, each of whom shall be a licensed attorney and registered mediator in Florida. The recipient Party shall select from such list one individual to act as mediator in the dispute set forth by the notifying Party. Neither Party shall be bound by any recommendation of the mediator; however, any agreement reached during mediation shall be final and conclusive. Each Party shall be responsible for payment of half of the mediator's fee, and is further responsible for its own travel costs to and from the mediation in Florida. Proper venue for the Mediation shall be Monroe County, Florida.

12.2 Any dispute arising hereunder is subject to the laws of Florida subject to all applicable Federal and state statutes and regulations thereunder. Venue for any action or proceeding shall lie with the 16th Judicial Circuit, in and for Monroe County, Florida and the Federal District Court in the Southern District of Florida, where applicable. The prevailing party shall be entitled to a reasonable attorney's fees and costs incurred as a result of any action or proceeding under this Agreement.

12.3 In the event that a Third Party commences or institutes legal proceedings against Oxitec and/or FKMCD in an attempt to stop or challenge the performance of the Investigation, Oxitec agrees to defend, indemnify, and hold harmless FKMCD and any of their agents and employees for such claims

12.4 Should the Investigation be terminated prematurely as a result of an event of Force Majeure (as defined in clause 13.3) or by agreement of the Parties pursuant to Clause 11.2, Oxitec may continue to use the Insectary if the FKMCD Board determines it is in the best interest(s) of the District and may charge a fair market rate for rental of the space by Oxitec for the purposes of rearing and supplying the Oxitec Technology to one or more Third Parties or otherwise.

13. GENERAL

13.1 This Agreement may only be amended in writing signed by duly authorized representatives of each Party.

13.2 No failure or delay on the part of either Party to exercise any right or remedy under this Agreement shall be construed or operate as a waiver thereof, nor shall any single or partial exercise of any right or remedy preclude a further exercise of such right or remedy.

13.3 Neither Party shall have any liability or be deemed to be in breach of this Agreement for any delays or failures in performance of this Agreement that results from an event or circumstances beyond the reasonable control of that Party, including without limitation civil protests or Third Party litigation directed against a Party with a view to bringing the Investigation to a premature end (an event of "*Force Majeure*"). The Party affected by such an event of *Force Majeure* shall:

(a) notify the other Party in writing when such event or circumstances cause a delay or failure in performance and when they cease to do so; and

(b) use its reasonable endeavors to avoid or remove the causes of non-performance and shall continue performance as expeditiously as possible as soon as such causes have been removed; (c) liaise with the other Party regarding the event or circumstances and the action to be taken by the Parties as a consequence.

If any *Force Majeure* event prevents a Party from performing its material obligations under this Agreement for three (3) months, that Party shall refer the issue to the Steering Committee which will be responsible for determining how the Parties will resolve matters if possible. In no event will such determination require the expenditure of funds by FKMCD, including defense of any lawsuit.

13.4 If any provision or part of this Agreement is held to be invalid, amendments to this Agreement may be made by the agreement of the parties to the addition or deletion of wording as appropriate to remove the invalid part of provision that otherwise retain the provision and the other provisions of this Agreement to the maximum extent permissible under applicable law.

13.5 In this Agreement the headings are used for convenience only and shall not affect its interpretation; references to persons shall include incorporated and unincorporated persons; references to the singular include the plural and vice versa; and references to the masculine include the feminine; references to Clauses and Schedules mean clauses of, and schedules to, this Agreement; references in this Agreement to termination shall include termination by expiry; and where the word "including" is used it shall be understood as meaning "including without limitation".

13.6 Except for the rights of the Indemnified Parties, this Agreement does not create any right enforceable by any person who was not a party to it. Furthermore, no person except a Party to this Agreement has any right to prevent the amendment of this Agreement or its termination.

13.7 This Agreement and its Schedule sets out the entire agreement between the Parties relating to the subject matter and supersedes all prior oral and/or written agreements, arrangements or understandings between them relating to such subject matter except the letter signed on 02 September 2014 relating to property ownership and division. Subject to Clause 10, the Parties acknowledge that they are not relying on any representation, agreement, term or condition which is not set out in this Agreement.

13.8 Neither Party shall act or describe itself as the agent or representative of the other, nor shall it make or represent that it has authority to make any commitments on the other's behalf.

13.9 The validity, construction and performance of this agreement shall be governed by the laws of the State of Florida and the Parties submit to the non-exclusive jurisdiction of the courts of Florida and venue of Monroe County, Florida in respect of any matter arising hereunder and not resolved in accordance with clause 12.1 except that a Party may seek an interim injunction in any court of competent jurisdiction.

13.10 This Agreement amends and restates the 2016 conditional Investigation Agreement. In the case of any discrepancy between the 2016 conditional Agreement and this Agreement, this Agreement shall control.

Accepted and agreed by the Parties through their authorized signatories:

For and on behalf of **Oxitec Ltd**

Signature ……..….

Print name Grey Frandsen …….

Title CEO ……...

Date 3rd September 2020 ……

For and on behalf of **Florida Keys Mosquito Control District**

Signature ……..…….

Print name Andrea L. Leal …….

Title Executive Director

Date 18 August 2020

Schedule 1

Proposed Field Trial Protocol

This protocol sets out the anticipated experimental details of the proposed field trial and is in compliance with regulatory approvals and associated requirements received as of June 2020. If required for technical, operational, regulatory, or other reasons, the Steering Committee may approve amendments to this protocol at any time.

Introduction

Aedes aegypti is a known vector for human diseases associated with Zika, dengue, and chikungunya viruses. Oxitec's novel approach to mosquito control uses the release of male OX5034 mosquitoes carrying a "female-specific self-limiting gene" to mate with wild females. When male OX5034 *Aedes aegypti* homozygous for the self-limiting gene (carrying two copies of the gene) are released into the environment and mate with wild *Aedes aegypti* females, their offspring inherit a single copy of the self-limiting gene (so are hemizygous). The self-limiting gene kills only female offspring (carrying one copy of the self-limiting gene), which die at early larval stages of development, while hemizygous males will survive to pass the OX5034 genes on to subsequent generations. Laboratory tests show that 100% of the resulting female offspring will die before reaching adulthood. Hence the OX5034 mosquito can be considered a sex- and species-specific larvicide targeting only female *Aedes aegypti*.

The over-arching purpose of the study is to assess and document a range of biosafety and efficacy metrics that will enable regulators and certain stakeholders to evaluate the potential of this product as a vector control tool for *Aedes aegypti* in the US.

Study Details

The precise location(s) of the trial site(s) and related plots are yet to be determined and will be confirmed by the Steering Committee.

The EUP trial design is divided into two study designs (Trial A and Trial B). These may take place simultaneously or in sequence as decided by the Steering Committee.

Trial A

The objectives of the Field Trial A will be to quantify various parameters from a single release point.

Site selection will be based on specific criteria.

Trial A Site selection criteria

All sites will comply with the following criteria:

- Total study area: minimum of 25 and maximum of 200 acres. These areas are based on the expected distribution of male *Aedes aegypti* from a single release point. For example, if the maximum distance travelled is ~180 m, that equates to a circle with an area of 25 acres based around a single mosquito release point. If the maximum distance travelled is ~500 m, that equates to a circle with an area of 200 acres based around a single mosquito release point. Most studies have found the maximal distance travelled by wild *Aedes* to be between 82 and 400m, this being heavily influenced by climatic conditions, presence of vegetation and the availability of breeding sites (Reiter et al., 1995; Muir & Kay, 1998; Russell et al., 2005). Previous field releases of OX5034 male mosquitoes in Brazil have recorded maximum dispersal distances of 198 m.
- As requested by EPA, trial areas will be separated by at least 500m and if mosquitoes are trapped at the perimeter of a Trial A area, then additional ovitraps will be installed at distances greater than 400 m from the release site to capture any mosquitoes that may travel further. These additional traps may be constrained in terms of direction by available land mass, although every effort will be made to accommodate the distances required. Water bodies such as canals or ponds up to approximately 100m across will be considered not to impact dispersal.
- Confirmed presence of *Aedes aegypti* (based on surveillance data).
- Available documentation of mosquito abatement (other than experimental treatment) during the period of study. Treated and untreated areas of the EUP will be chosen to be as similar as possible, including in terms of any known mosquito abatement activity.
- The outer boundary of the trial area (denoted by the traps furthest from the central release point) will be greater than 500 m from commercial citrus growing areas and from sewage treatment plants.

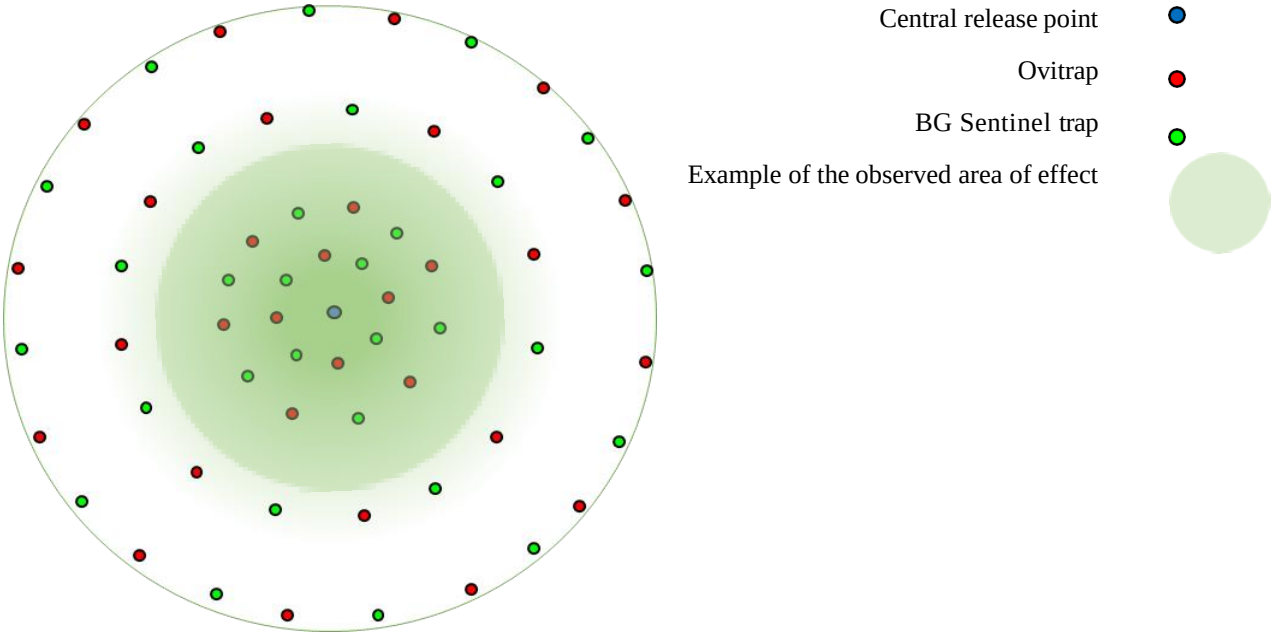

Figure 1. Schematic overview of a trial site for Trial A showing the central release point and a potential arrangement of 30 x egg traps (ovitraps) and 30 x adult traps (BG Sentinel® traps). Traps will typically be located between 25 and 400 meters from the central release point, although the maximum distance may be less dependent on the available landmass. Please note that traps may not be positioned precisely in concentric rings as shown.

Table 1. No of sites, application rates (doses 1-3 i.e. lowest - highest), and replicates for Trial A, including the treated acreages and life-stages assessed.

Trial	**Location***	**Number of untreated areas (Required)**	**Number of treated areas (dose 1 - low) (Required)**	**Number of treated areas (dose 2 - medium) (Optional)**	**Number of treated areas (dose 3 - high) (Optional)**	**Maximum acreage per trial site**	**Maximum total treated acreage**	**Life stage assessed**
Trial A	Florida - Monroe County	3	3	3	3	200	1800	Eggs or adults (one life-stage only)

OX5034 transport

Known quantities of OX5034 eggs or adults will be delivered to release site(s) in triple layered containment. Ambient temperature within the vehicle should not exceed 86°F (30°C) during storage or transport. If the temperature is higher than 86°F (30°C), cooling aids (e.g. air-conditioning or ice packs) may be used, but minimum temperatures should not be lower than 15°C for eggs or 22°C for adults.

Application of OX5034 treatment

Two different release modes for OX5034 are envisaged for this EUP, viz. egg and adult release modes. The aim is to test the use of Mosquito Rearing Boxes, which enable the deployment of OX5034 mosquito eggs in specially designed Mosquito Rearing Boxes which facilitate egg-to-adult development in the field. We also may benefit from rearing OX5034 male adults for release (produced in a rearing facility without the use of tetracycline) to test dispersal and/or efficacy of OX5034 male adults in US field conditions. Further details of each of these release modes are provided below. In all cases, the locations of each Mosquito Rearing Box/event will be given a unique identifier and georeferenced for accurate placement and mapping.

OX5034 Mosquito Rearing Boxes

At the prescribed release locations, in the case of egg releases prescribed amounts of water, mosquito food, and other additives will be added to Mosquito Rearing Boxes. A known quantity of OX5034 eggs will also be added to each Mosquito Rearing Box. Adult males of the desired quantity (anticipated 500-2,500 male adults per Mosquito Rearing Box) will emerge within 22 days of the Mosquito Rearing Box setup and deployment.

OX5034 Adult Release

In the case of adult releases, known quantities of adults (already contained in pots or cages) will be allowed to acclimatize and rest for >10 minutes prior to release.

Field Monitoring Methods

Fluorescent Marker and PCR assessments

The fluorescent marker is readily visible in all life-stages apart from eggs and will be used for OX5034 identification. Molecular analyses by PCR will be used to validate marker identifications in a minimum number of 40 fluorescent and 40 non-fluorescent screened individuals. It is expected that this will be required only once, to ensure accurate identification by trial staff. In addition, all individuals will be taxonomically identified to genus and/or species level. Fluorescence screening will also be used to assess penetrance of the female-specific self-limiting gene.

Please note that field-collected samples of *Aedes aegypti* may be taken and stored for subsequent analyses of genetic diversity and introgression of background genes.

Eggs

Ovitraps are a commonly used system for collecting *Ae. aegypti* mosquito eggs, mimicking natural breeding sites in which females lay eggs. Ovitraps consist of a pot containing water and a substrate (paper or wood) protruding above the water line on which eggs can be laid. The substrate used will be consistent across replicates and plots. Ovitraps will be positioned in sheltered locations, typically nearby residential, commercial, or utility premises. Appropriate consent for the placing and servicing of the traps will be obtained. Each trap will have a unique identifier and georeferenced for accurate placement and mapping.

A minimum of 30 ovitraps per plot for Trial A will be distributed across the trial area. Trapping intervals will typically be 7 days (maximum 9 days), at which time the water and oviposition substrate will be replaced, or the trap may be substituted for a new one. Oviposition substrates will be labelled and stored

individually to prevent cross contamination during transport. Once at the laboratory they are dried at room temperature for a minimum of 2 days (maximum 14 days) to mature the eggs prior to hatching.

Ovitrap Density

The trapping density we recommend when used as surveillance tool is a minimum of 28 per site. This minimum number of traps per site (28) was calculated as the sample size required for multiple regression to detect a medium-sized effect (Cohen's $f^2 = 0.25$) with 80% statistical power when there are 4 predictor variables. This number was calculated using the computer program G*Power. A similar ovitrap density or higher has been used successfully previously (Harris et al., 2012; Gorman et al., 2015; Carvalho et al., 2015) and is not expected to confound or interfere with any measurements of efficacy. For Trial A, we propose using a minimum of 30 ovitraps per area through pre-release and treatment periods, increasing the number to a minimum of 48 per area during post-release monitoring periods, during which we will also increase the monitoring area by extending the distance from the center to the perimeter by 100m in all directions.

Ovitrap Interval

The trapping interval we recommend for ovitraps when used as surveillance tool is weekly. This has been chosen as it permits constant trapping throughout the trial period yet strikes a balance between the maximum number of data points we could collect and a trapping interval that does not become a frustration to homeowners and offers operationally feasible surveillance.

Adult female traps

BG-Sentinel® traps (Biogents, Germany) target both male and female adults of several Aedine species. They employ a combination of visual and olfactory (odors and/or CO_2) attractants to lure individuals towards a motorized fan and into a catch-bag. Power can be supplied by mains, battery or solar generated electricity. BG-Sentinel® traps will be positioned in sheltered locations, typically nearby residential, commercial, or utility premises. Appropriate consent for the placing and servicing of the traps will be obtained. Each trap will have a unique identifier and be georeferenced for accurate placement and mapping.

A minimum of 30 BG traps per plot for Trial A will be distributed across the study area. Locations of BG-Sentinel® trap units will be rotated to prevent bias between individual traps. The catch-bag in BG-Sentinel® traps can be changed daily, every few days or weekly. Trapping intervals will be the same across plots and will be a maximum of 9 days. Catch-bags will be labelled and stored individually to prevent cross contamination during transport. Once at the laboratory samples will be processed within 96 hours.

Adult Female Trapping Density

The trapping density we recommend when used as a surveillance tool evaluating changes in abundance is a minimum of 28 per area. However, for Trial A we propose using a minimum of 30 BG-Sentinel® traps per area. This will apply throughout the treatment period. During post-release monitoring periods only ovitraps will be used to detect disappearance of the transgene from the environment. This minimum number of BG traps per area (28) was calculated as the sample size required for multiple regression to detect a medium-sized effect (Cohen's $f^2 = 0.25$) with 80% statistical power when there are 4 predictor variables. This number was calculated using the computer program G*Power. Were too many of our released adults caught in BG-Sentinel® traps, this could reduce or interfere with the performance results obtained. Mark

release recapture results to date in Brazil have shown that BG Sentinel® traps in direct line of site and in close proximity to the release point, when combined with point release of adults can catch a high proportion of released individuals. Therefore, care will be taken to ensure BG-Sentinel® traps are located appropriately and not in a direct line of site to release locations.

Adult Female Trapping Interval

The trapping interval we propose for BG-Sentinel® traps during Trial A is weekly, every few days, or daily. Weekly is sufficient for measurements of dispersal and daily allows the most accurate estimates of longevity.

Untreated comparator areas

For Trial A, untreated areas will be utilized to provide samples of larvae for mortality assessments that have not been exposed to any form of treatment. These areas will be of similar size and characteristics to treated areas; where possible, comparator and treatment areas will be randomly allocated. The number of untreated areas will be the same as the number of areas for each treatment rate. For Trial A this will be at least three. Untreated areas will be at least 500 m away from treatment areas.

Objective of the Program

Trial A

The objectives of the Field Trial A will be to quantify from a single release point:

- Efficacy of the active ingredient (% mortality observed in fluorescent female progeny compared with untreated, i.e. non-fluorescent females).
- The adult over-flooding ratio achieved i.e. Oxitec males:wild male ratio (using BG traps).
- The proportion of treated i.e. fluorescent individuals within each ovitraps (mating fraction).
- Dispersal distance of released adult male OX5034 mosquitoes (maximum and mean flight distances from the central release point observed by BG trap catches).
- Dissemination distance of the transgene (maximum distance that fluorescent individuals are found from the central release point observed by ovitrap catches).
- Duration and scale of residual activity (time until disappearance of adult males and fluorescent larvae, and the rate of disappearance in the environment measured until no individuals have been found for a minimum of 10 consecutive weeks i.e. a period sufficient for at least two discrete generations.

Application

It is anticipated that for eggs or adults the interval between applications would be <22 days. The longest interval anticipated between releases/deployments of Mosquito Rearing Boxes will be evaluated. Target application rates will be fixed for the duration of the releases. In some cases, the effects of a single box deployed may be assessed and in some cases a series of consecutive releases will be assessed. For efficacy metrics, consecutive weekly releases will be used.

In either case, the maximum weekly release rates will be 20,000 males per acre for Trial A (maximum of 20,000 males total per area per week as Trial A is a single release point). We anticipate that Trial A would be completed at a minimum of one application rate (with 3 replicates) not including untreated comparator sites.

Mortality assessments

Eggs from each ovitrap will be induced to hatch (to synchronize hatching) then screened for fluorescence and counted within 24 hours. Larvae will be reared under laboratory conditions at 27°C [+/- 2°C], 70% [+/- 10%] relative humidity, 12h: 12h light: dark cycle and fed *ad libitum*. Once pupated, remaining individuals will be placed into cages for adult emergence. Post-emergence, all adults will be taxonomically identified to species level, screened for fluorescence, and sexed. Note, a minimum number of 40 fluorescent and 40 non-fluorescent *Ae. aegypti* will undergo molecular identification by quantitative PCR to complete a one-time validation of the fluorescence screening by confirming their genotype as either OX5034 or wild *Aedes aegypti*. This may require a repeat procedure should this molecular assay fail for any reason.

Persistence Measurements

OX5034 mosquitoes possess a self-limiting gene and a fluorescent marker gene. The self-limiting gene, when passed onto offspring, prevents female progeny from surviving to functional adulthood in the absence of tetracycline. By design, male offspring survive and can develop through to adulthood and potentially mate with wild females. OX5034 genes are therefore passed down as a single copy from male parents only, and as they are subject to normal Mendelian inheritance patterns, are not expected to establish at the proposed trial site but decline predictably following the cessation of releases over the course of <10 generations.

Ovitrap data will be used to quantify the presence (anticipated decline) of the fluorescence gene over time. Monitoring will continue until at least 10 consecutive weeks without the presence in ovitraps of OX5034 fluorescent mosquitoes. Given that the generation time for *Aedes aegypti* is usually 4 weeks or less, this period should be sufficient to allow two discrete generation times without fluorescence. Note, a minimum number of 40 fluorescent and 40 non-fluorescent *Ae. aegypti* will undergo molecular identification by quantitative PCR to complete a one-time validation of the fluorescence screening by confirming their genotype as either OX5034 or wild *Aedes aegypti*. This may require a repeat procedure should this molecular assay fail for any reason.

Male Dispersal Measurements

The dispersal distance of adult male OX5034 will be assessed within Trial A.

- Each OX5034 Mosquito Rearing Box (containing eggs) or release pot (adults) will have contained a known quantity of individuals prior to release and samples will be inspected post-release to estimate the actual number of released males.
- OX5034 adult males are inherently marked by the fluorescent protein, but to distinguish between released homozygous males and hemizygous males of subsequent generations, if required release cohorts will be marked using fluorescent powders. In the case of adults, this will be done by agitating the insects in a closed container that has been coated on the inside

with fluorescent powder prior to release. In the case of eggs, the inside surfaces of the release device will be coated in the fluorescent powder, enabling the adults to contact the powder prior to emergence from the box. The males (whether released as eggs or adults) will be released from a single point source, either as a single release (adults) or in a sustained manner over a period of several weeks (eggs).

- To monitor dispersal a network of BG Sentinel® traps (minimum of 30) will be positioned to a distance of up to 400m depending on available land area. Catch bags will be collected and replaced between daily (maximum frequency) or weekly (minimum frequency). Trapped mosquitoes will be screened for fluorescence and identified as marked males (OX5034), unmarked males (WT) and unmarked females (WT). The trapping period extends from the time of the first release until three consecutive days without recaptures of powder-marked males. The mean and maximum dispersal distances of OX5034 adult males will be calculated. If dispersal data are not normally distributed, median and maximum values, and interquartile range will be reported.

Data Analysis Methods

Efficacy data analyses are subject to ongoing discussions with EPA and will also be subject to Steering Committee approval. It is anticipated that the statistical methods, as outlined below, will be used to analyze data, and additional data analyses may also be carried out in support of product registration under FIFRA Section 3.

Efficacy

The evaluations of each replicate will yield survival data, i.e., number of females surviving (reaching adulthood). Therefore, the recommended[1] calculation to account for survival rates in untreated replicates is an adaption of Mulla's formula.[2] The output of this formula is the control adjusted percentage mortality (efficacy):

E=100*((C-T)/C) or E=100*(1-T/C)

where:

E = percentage efficacy in individual ovitraps from the treated area.

C = percentage of untreated females surviving across all ovitraps in control areas.

T = percentage of treated, i.e. fluorescent females surviving in individual ovitraps.

[1] *Guidelines for laboratory and field testing of mosquito larvicides. Editors: Dr M. Zaim/WHOPES, 39 p., Publication date: June 2005. WHO reference number: WHO/CDS/WHOPES/GCDPP/2005.13*

[2] *Mulla MS, Darwazeh HA. Activity and longevity of insect growth regulators against mosquitoes. Journal of Economic Entomology, 1975, 68:791–794.*

Trial A replication

We anticipate that in each climate zone utilized, Trial A would evaluate a minimum of one application rate and untreated controls with each being replicated at least three times (minimum of six sites in total).

Test Acceptance Criteria

Each of the efficacy studies (i.e. data from any single plot) will be considered valid providing:

- The total number of larvae (sum of fluorescent and non-fluorescent) collected from all ovitraps over the course of the study is equal to or greater than 100.

The adult male OX5034 dispersal experiment will be determined as valid providing:

- The total number of marked (i.e. released) OX5034 fluorescent male adults that are recovered over the course of the study, is greater than 20.

Statistical Analysis

Efficacy

We will assess differences in the numbers of females surviving between release and non-release treatments, as well as how survival is affected by the following variables:

- Release rate (the number of male adults released/exiting a single mosquito rearing box)
- Trap distance (how far the trap is from the point of release)
- Site (which site replicate is being measured)

We will assess the difference in female survival between release and non-release sites using general linear mixed-effects models (GLMM) with the random effect of site, a crossed random effect of trap distance, and the covariates life stage and release rate. The model will use a quasibinomial distribution and a logit link function since the response variable is recorded as a percentage. Percent efficacy and 95% confidence intervals will be calculated from the results of the GLMM. The efficacy (E) of OX5034 to kill female mosquitoes is calculated using an adaption of Mulla's formula:

$$E=100*((C-T)/C) \textit{ or } E=100*(1-T/C)$$

E = percentage efficacy in individual ovitraps from the treated area.

C = percentage of untreated females surviving across all ovitraps in control areas.

T = percentage of treated, i.e. fluorescent females surviving in individual ovitraps.

Persistence Monitoring

The Kaplan-Meier estimator will be used to characterize the persistence of the OX5034 gene in release sites. Estimated median values, 95% confidence intervals, interquartile ranges and maxima will be reported.

Trial B

Trial B Site selection criteria

The objectives of the Field Trial B will be to quantify various parameters across multiple release points. All sites (both treated and untreated controls) will comply with the following criteria:

- Total trial area: minimum of 10 and maximum of 80 acres (FL). The Trial B defined areas are smaller than for Trial A, because the release point spacing will be based on the dispersal/coverage determined in Trial A or in previous trials in other locations, e.g. Brazil.
- Confirmed presence of *Aedes aegypti* (based on surveillance data).
- Available documentation of mosquito abatement (other than experimental treatment) during the period of study. Treated and untreated areas of the EUP will be chosen to be as similar as possible, including in terms of any known mosquito abatement activity.
- The distance between trial locations (i.e., control and treated locations) will be at least 500 m. Dispersal distances measured from egg releases from the Mosquito Rearing Boxes will be used to support dispersal distances for Trial B.
- The outer boundary of the trial area (denoted by the traps furthest from the central release point) will be greater than 500 m from commercial citrus growing areas or sewage treatment plants.
- Final site selections will aim to provide sites that are similar in terms of mosquito pest pressure (abundance), based on mean number of larvae per trap per week.

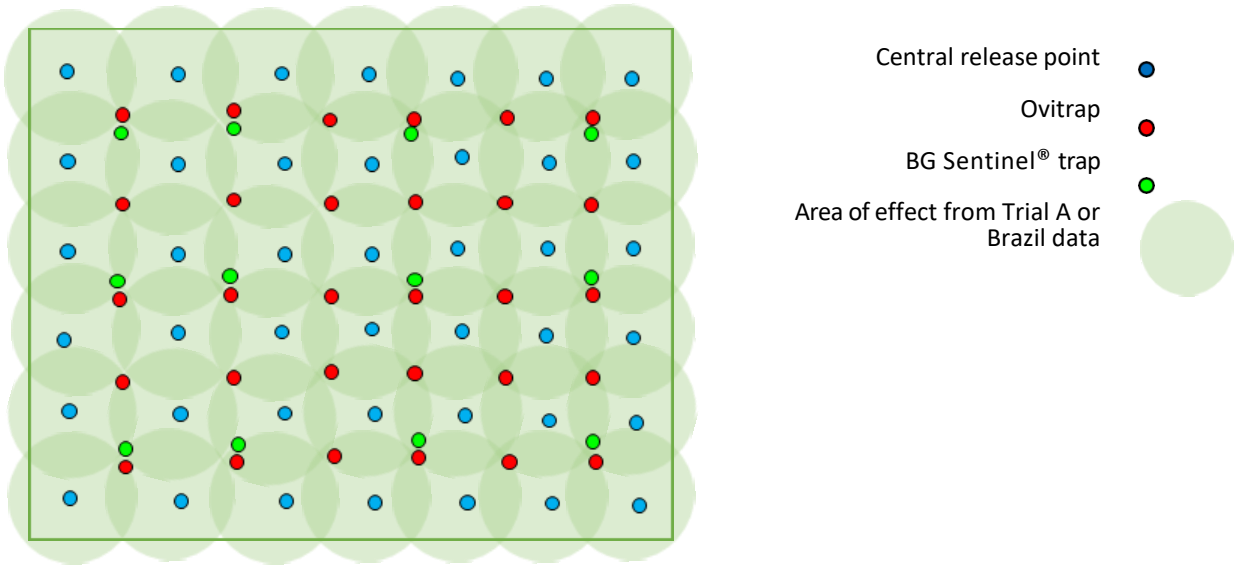

Figure 9. Schematic overview of a trial site for Trial B showing the multiple release points and a potential arrangement of egg traps (ovitraps, in red) and adult traps (BG Sentinel® traps, in green). The observed area of effect from Trial A and/or data generated from trials in Brazil will be used to inform the release point locations for Trial B. The number of release points shown (36) is for illustrative purposes only.

General Experimental Methods

OX5034 transport

Known quantities of OX5034 eggs will be delivered to release site(s) in triple layered containment. Ambient temperature within the vehicle should be between 59°F (15°C) and 86°F (30°C) during storage or transport of eggs. If the temperature is higher than 86°F (30°C), cooling aids (e.g. air-conditioning or ice packs) may be used.

Application of OX5034 treatment

The aim for Trial B is to test the use of Mosquito Rearing Boxes, which enable the deployment of OX5034 mosquito eggs in specially designed Mosquito Rearing Boxes which facilitate egg-to-adult development in the field. In all cases, the locations of each Mosquito Rearing Box/event will be given a unique identifier and georeferenced for accurate placement and mapping.

OX5034 Mosquito Rearing Boxes

At the prescribed release locations, in the case of egg releases prescribed amounts of water, mosquito food, and other additives will be added to Mosquito Rearing Boxes. A known quantity of OX5034 eggs will also be added to each Mosquito Rearing Box. Adult males of the desired quantity (anticipated 2,500 male adults per Mosquito Rearing Box[3]) will emerge within 22 days of the Mosquito Rearing Box setup and deployment.

Construction

- Component parts will be safe to handle, nontoxic to rearing process, robust and capable of withstanding local environmental conditions for at least 22 days.
- Protected from applications of insecticide, in particular of *Bti* (*Bacillus thuringiensis israelensis*), as far as is possible.
- Option to fix to typical urban landscape but can be used as a free-standing Mosquito Rearing Box.
- Easy and environmentally friendly disposal – safe and simple mess-free draining of water, with no parts left behind.
- The complete Mosquito Rearing Box will be weatherproof and also ensure environmental control of water temperature, condensation and light conditions to enable efficient mosquito development.
- For the purposes of the trial, Mosquito Rearing Boxes will be physically isolated from the public to prevent vandalism/tampering, or where that is not possible, located discretely and out of public view.
- Mosquito Rearing Box design will preclude the Mosquito Rearing Box becoming a breeding site for wild mosquitoes.

[3] Mosquito Rearing Boxes designed to produce other numbers of male mosquitoes, e.g. 500 males per box, 1,000 males per box, etc. may also be used.

Field Monitoring Methods

Fluorescent Marker and PCR assessments

The fluorescent marker is readily visible in all life-stages apart from eggs and will be used for OX5034 identification. Note, a minimum number of 40 fluorescent and 40 non-fluorescent *Ae. aegypti* will undergo molecular identification by quantitative PCR to complete a one-time validation of the fluorescence screening by confirming their genotype as either OX5034 or wild *Aedes aegypti*. In addition, all individuals will be taxonomically identified to genus and/or species level. Fluorescence screening will also be used to assess penetrance of the female-specific self-limiting gene.

Please note that field-collected samples of *Aedes aegypti* will be taken and stored for subsequent analyses of genetic diversity and introgression of background genes.

Eggs

Ovitraps are a commonly used system for collecting *Ae. aegypti* mosquito eggs, mimicking natural breeding sites in which females lay eggs. Ovitraps consist of a pot containing water and a substrate (paper or wood) protruding above the water line on which eggs can be laid. The substrate used will be consistent across trial sites. Ovitraps will be positioned in sheltered locations, typically nearby residential, commercial, or utility premises. Appropriate consent for the placing and servicing of the traps will be obtained. Each trap will have a unique identifier and georeferenced for accurate placement and mapping.

A minimum of 30 ovitraps per plot for Trial B will be distributed across the trial area. Trapping intervals will typically be 7 days (maximum 9 days), at which time the water and oviposition substrate will be replaced, or the trap may be substituted for a new one. Oviposition substrates will be labelled and stored individually to prevent cross contamination during transport. Once at the laboratory they are dried at room temperature for a minimum of 2 days (maximum 14 days) to mature the eggs prior to hatching.

Ovitrap Density

The trapping density we recommend when used as surveillance tool is a minimum of 28 per site. This minimum number of traps per site (28) was calculated as the sample size required for multiple regression to detect a medium-sized effect (Cohen's $f^2 = 0.25$) with 80% statistical power when there are 4 predictor variables. This number was calculated using the computer program G*Power. A similar ovitrap density or higher has been used successfully previously (Harris et al., 2012; Gorman et al., 2015; Carvalho et al., 2015) and is not expected to confound or interfere with any measurements of efficacy. For Trial B we propose using a minimum of 30 ovitraps per area through pre-release and treatment periods, increasing the number to a minimum of 48 per area during post-release monitoring periods, during which we will also increase the monitoring area by extending the distance from the center to the perimeter by 100m in all directions.

Ovitrap Interval

The trapping interval we recommend for ovitraps when used as surveillance tool is weekly. This has been chosen as it permits constant trapping throughout the trial period yet strikes a balance between the maximum number of data points we could collect and a trapping interval that does not become a frustration to homeowners and offers operationally feasible surveillance.

Adult female traps

BG-Sentinel® traps (Biogents, Germany) target both male and female adults of several Aedine species. They employ a combination of visual and olfactory (odors and/or CO_2) attractants to lure individuals towards a motorized fan and into a catch-bag. Power can be supplied by mains, battery or solar generated electricity. BG-Sentinel® traps will be positioned in sheltered locations, typically nearby residential, commercial, or utility premises. Appropriate consent for the placing and servicing of the traps will be obtained. Each trap will have a unique identifier and be georeferenced for accurate placement and mapping.

A minimum of 5 BG traps for Trial B will be distributed across the study area. Locations of BG-Sentinel® trap units will be rotated to prevent bias between individual traps. The catch-bag in BG-Sentinel® traps can be changed daily, every few days or weekly. Trapping intervals will be the same across plots and will be a maximum of 9 days. Catch-bags will be labelled and stored individually to prevent cross contamination during transport. Once at the laboratory samples will be processed within 96 hours.

Adult Female Trapping Density

The trapping density we recommend when used as a surveillance tool evaluating changes in abundance is a minimum of 28 per area. For Trial B they will not be used to evaluate changes in abundance and will only be used to evaluate overflooding (OX5034 male:wild male) and/or sex (male:female) ratios. These two metrics do not specifically relate to any product label claims but allow a preliminary assessment of the dosage applied, therefore a minimum of 5 per area is proposed. This will apply throughout the treatment period. During post-release monitoring periods only ovitraps will be used to detect disappearance of the transgene from the environment. Mark release recapture results to date in Brazil have shown that BG Sentinel® traps in direct line of site and in close proximity to release points, when combined with point release of adults can catch a high proportion of released individuals. Therefore, care will be taken to ensure BG-Sentinel® traps are located appropriately and not in a direct line of site to release locations.

Adult Female Trapping Interval

For Trial B we will service BG-Sentinel® traps weekly (maximum 9 days), as the primary metric will be assessing overflooding (OX5034 male:wild male) and/or sex (male:female) ratios. These two metrics do not specifically relate to any product label claims but allow a preliminary assessment of the dosage applied. This weekly interval has been chosen as it permits a less variable ratio to be obtained and strikes a balance between the maximum number of data points we could collect and a trapping interval that does not become a frustration to homeowners and offers operationally feasible surveillance.

Untreated comparator areas

For Trial B, untreated areas will be utilized to provide samples of larvae for mortality assessments that have not been exposed to any form of treatment. These areas will be of similar size and characteristics to treated areas; where possible, comparator and treatment areas will be randomly allocated. The number of untreated areas will be the same as the number of areas for each treatment rate. For Trial B this will be at least three.

Objective of the Program

The objectives of the Field Trial B will be to quantify across multiple release points:

- Efficacy of the active ingredient (% mortality observed in fluorescent female progeny compared with untreated, i.e. non-fluorescent females).
- The adult over-flooding ratio achieved i.e. Oxitec males:wild male ratio in each BG trap.
- The proportion of treated i.e. fluorescent individuals within each ovitrap (mating fraction).
- Duration and scale of residual activity (time until disappearance of fluorescent larvae, and the rate of disappearance in the environment measured until no individuals have been found for a minimum of 10 consecutive weeks i.e. a period sufficient for at least two discrete generations.
- The presence of fluorescent larvae in natural *Aedes aegypti* breeding sites, including those published as relevant in the US such as septic tanks, disused tires, flowerpots, planters, trivets (Hribar et al., 2004) and plastic buckets, trash cans, and discarded plastic containers (Hribar et al., 2001).

In total a minimum of one trial (with 3 replicates at each application rate) will be performed. The precise location(s) of the trial site(s) and related plots are yet to be determined and will be reported to the EPA before the protocol is initiated.

Efficacy Measurements: Trial B

Application

It is anticipated that for eggs or adults the interval between applications would be <22 days. The longest interval anticipated between releases/deployments of Mosquito Rearing Boxes will be evaluated. Target application rates will be fixed for the duration of the releases. The maximum weekly release rates will be 20,000 males per acre for Trial B (maximum of 1,600,000 males total per area per week as Trial B is limited to 80 acres in FL). We anticipate that in each climate zone utilized, Trial B would be completed at a minimum of one application rate (with 3 replicates) not including untreated comparator sites.

Mortality assessments

Eggs from each ovitrap will be induced to hatch (to synchronize hatching) then screened for fluorescence and counted within 24 hours. Larvae will be reared under laboratory conditions at 27°C [+/- 2°C], 70% [+/- 10%] relative humidity, 12h: 12h light: dark cycle and fed *ad libitum*. Once pupated, remaining individuals will be placed into cages for adult emergence. Post-emergence, all adults will be taxonomically identified to species level, screened for fluorescence, and sexed. A minimum number of 40 fluorescent and 40 non-fluorescent *Ae. aegypti* will undergo molecular identification by quantitative PCR to complete a one-time validation of the fluorescence screening by confirming their genotype as either OX5034 or wild *Aedes aegypti*. This may require a repeat procedure should this molecular assay fail for any reason.

Cryptic Breeding Sites

At least 6 natural breeding sites per area for Trial B will be identified and checked on a weekly cycle (maximum 9 days) for the presence of *Ae. aegypti*. No egg-laying substrate will be used as the intention is to examine 'natural' breeding sites and so collections will consist of larvae only. If found, larval samples of *Ae. aegypti* will be taken to the laboratory for screening of fluorescence to establish if they were fathered by OX5034 males. It is anticipated that any fluorescent larvae collected would therefore themselves be males, as fluorescent females are expected to die at early larval stages. These collections would not

contribute to efficacy or other measurements. Descriptions of the types of natural breeding site, locations, and larval counts will be provided.

Persistence Measurements

OX5034 mosquitoes possess a self-limiting gene and a fluorescent marker gene. The self-limiting gene, when passed onto offspring, prevents female progeny from surviving to functional adulthood in the absence of tetracycline. By design, male offspring survive and can develop through to adulthood and potentially mate with wild females. OX5034 genes are therefore passed down as a single copy from male parents only, and as they are subject to normal Mendelian inheritance patterns, are not expected to establish at the proposed trial site but decline predictably following the cessation of releases over the course of <10 generations.

Ovitrap data will be used to quantify the presence (anticipated decline) of the fluorescence gene over time. Monitoring will continue until at least 10 consecutive weeks without the presence in ovitraps of OX5034 fluorescent mosquitoes. Given that the generation time for Aedes aegypti is usually 4 weeks or less, this period should be sufficient to allow two discrete generation times without fluorescence. Note, a minimum number of 40 fluorescent and 40 non-fluorescent *Ae. aegypti* will undergo molecular identification by quantitative PCR to complete a one-time validation of the fluorescence screening by confirming their genotype as either OX5034 or wild *Aedes aegypti*. This may require a repeat procedure should this molecular assay fail for any reason.

Data Analysis Methods

Efficacy data analyses are subject to ongoing discussions with EPA and will also be subject to Steering Committee approval. It is anticipated that the statistical methods, as outlined below, will be used to analyze data, and additional data analyses may also be carried out in support of product registration under FIFRA Section 3.

Efficacy

The evaluations of each replicate will yield survival data, i.e., number of females surviving (reaching adulthood). Therefore, the recommended[4] calculation to account for survival rates in untreated replicates is an adaption of Mulla's formula.[5] The output of this formula is the control adjusted percentage mortality (efficacy):

E=100*((C-T)/C) or E=100*(1-T/C)

where:

[4] *Guidelines for laboratory and field testing of mosquito larvicides. Editors: Dr M. Zaim/WHOPES, 39 p., Publication date: June 2005. WHO reference number: WHO/CDS/WHOPES/GCDPP/2005.13*

[5] *Mulla MS, Darwazeh HA. Activity and longevity of insect growth regulators against mosquitoes. Journal of Economic Entomology, 1975, 68:791–794.*

E = percentage efficacy in individual ovitraps from the treated area.

C = percentage of untreated females surviving across all ovitraps in control areas.

T = percentage of treated, i.e. fluorescent females surviving in individual ovitraps.

Trial B replication

We anticipate that in each climate zone utilized, Trial B would evaluate a minimum of one application rate and untreated controls with each being replicated at least three times (minimum of six sites in total).

Test Acceptance Criteria

For each of the efficacy studies (i.e. data from any single plot) will be considered valid providing:

- The total number of larvae (sum of fluorescent and non-fluorescent) collected from all ovitraps over the course of the study is equal to or greater than 100.

Statistical Analysis

Efficacy

We will assess the difference in number of the percentage of females surviving between release and non-release treatments, as well as how survival is affected by the following variables:

- Release rate (the number of male adults released/exiting a single mosquito rearing box)
- Trap distance (how far the trap is from the point of release)
- Site (which site replicate is being measured)

We will assess the difference in female survival between release and non-release sites using general linear mixed-effects models (GLMM) with the random effect of site, a crossed random effect of trap distance, and the covariates life stage and release rate. The model will use a quasibinomial distribution and a logit link function since the response variable is recorded as a percentage. Percent efficacy and 95% confidence intervals will be calculated from the results of the GLMM. The efficacy (E) of OX5034 to kill female mosquitoes is calculated using an adaption of Mulla's formula:

$$E=100*((C-T)/C) \textit{ or } E=100*(1-T/C)$$

E = percentage efficacy in individual ovitraps from the treated area.

C = percentage of untreated females surviving across all ovitraps in control areas.

T = percentage of treated, i.e. fluorescent females surviving in individual ovitraps.

Persistence Monitoring

The Kaplan-Meier estimator will be used to characterize the persistence of the OX5034 gene in release sites. Estimated median values, 95% confidence intervals, interquartile ranges and maxima will be reported.

Long-range testing plans

It is anticipated that trial(s) will be initiated in 2020, pending regulatory approval, and that OX5034 trials will be completed within 24 calendar months of initiation.

Method of Disposition:

Any OX5034 *Aedes aegypti* not utilized in the program will be killed by freezing and then disposed of in general waste. In addition, any fluorescent larvae hatched from ovitraps, or fluorescent adults from BG traps, once transported to the lab for identification, will also be disposed of by freezing at <15 °C for 12 hours or longer, and then disposed of in general waste.

Deviations

Any deviations to this protocol are identified in writing and reported to the Head of Field Operations for review. Deviations will be investigated, tracked through to closure and reported in the final study report.

List of Acronyms, Abbreviations and Technical Terms

WT = wild type

tTAV = tetracycline-repressible transactivator variant protein

N/A = not applicable

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Schedule 2

Both Parties will provide certain equipment to enable the Project to proceed. The lists for each Party below cover the main items but are not intended to be exhaustive.

Provided by Oxitec

Item	Quantity
BG traps	**Minimum 270 (all traps required)**
Ovitraps	**Minimum 400 (all traps required)**
Fluorescence stereo microscope	**1**
Stereo microscope	**1**
Weighing scales	**1**
Incubator (for egg storage)	**1**
Temperature loggers (buttons)	**20**
Humidity loggers (buttons	**10**
Laptop computer	**1**
Fridge	**1**
Freezer	**1**
Sieves (fine to capture eggs)	**3**
Release devices	**Minimum 200 (all devices required)**
Release device liners	**Minimum 1200 (all liners required)**

Provided by FKMCD

- Use of an existing FKMCD truck which is of suitable size to transport the release devices to the release site, for example a Ford F150 or equivalent.
- An already existing FKMCD incubator will also be provided in the monitoring laboratory for the rearing of larvae from the field.

Schedule 3

Oxitec shall supply the following tangible components of the Materials plus intangible know-how.

- Eggs of genetically engineered OX5034 *Aedes aegypti* mosquito.
- Standard Operating Procedures relating to the use of OX5034 in the Protocol including without limitation the handling and release of the strain and product.

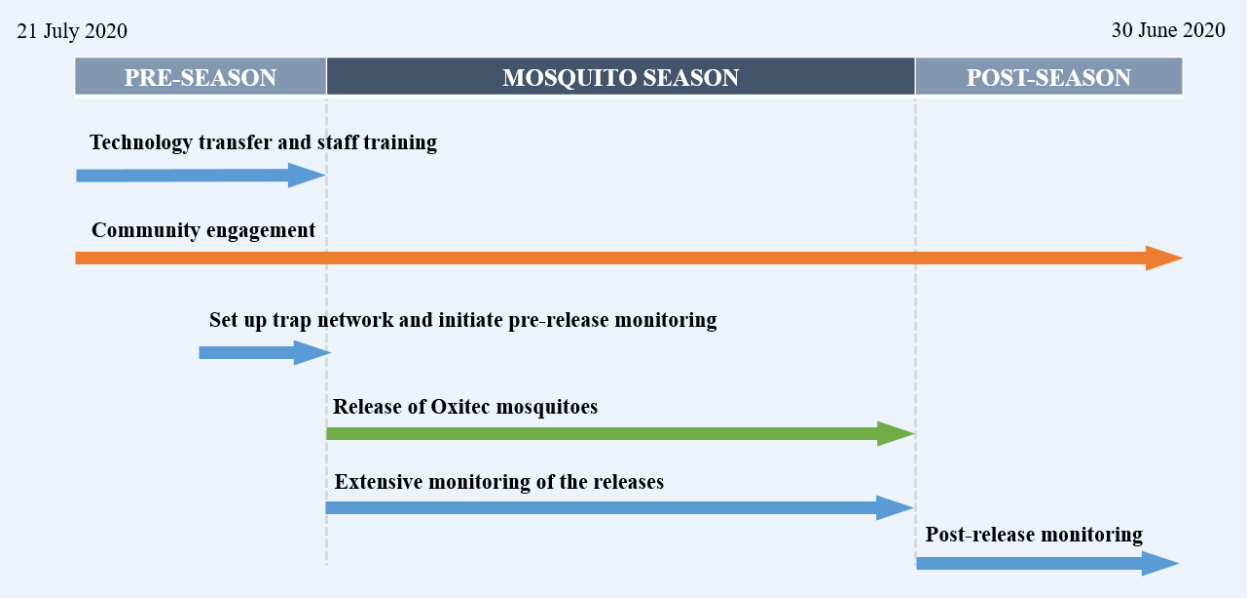
Schedule 4

The main elements of the Work Plan are the following:

- Technology transfer and staff training
- Community Engagement
- Baseline mosquito surveillance
- Release of OX5034 mosquitoes
- Ongoing mosquito surveillance
- Post-release mosquito surveillance

Workstreams within each of these areas will be undertaken in support of activities in relation to the implementation of protocols as detailed in Schedule 1.

An anticipated timeline for each of the main elements of the Work Plan is shown below and will be formalized within the Steering Committee at the outset of the project. In general, the project window during which the workplan will be conducted lies between 21 July 2020 and 30 June 2022. Precise timings will be subject to Steering Committee discussion and approval. Regulatory considerations may necessitate the project to be extended (for example to complete post-release monitoring obligations). The timelines will be routinely assessed by the Steering Committee throughout the project and may be adjusted.



Primary Work Plan components shown as an anticipated project timeline within the project window of 21 July 2020 to 30 June 2022.