2nd Delta MVCD-Oxitec Public Educational Webinar, May 24th 2022

Oxitec’s Scientific Publications, Independent Validation, and Data Transparency
Introductions – Panelists With You Today

Rajeev Vaidyanathan
Director of U.S. Programs
Oxitec

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Chief Development Officer
Oxitec
Delta MVCD and Oxitec are hosting a series of public educational webinars to share information with residents of Tulare County and provide forums to answer questions.

- Webinars are open to everyone.
- Webinars are recorded and made available for everyone after the event.
- All questions relating to the webinar topic(s) will be answered (some in batches if questions are similar).
- If time runs out, we will accept questions in writing via info@oxitec.com.
- Questions and answers will be published in writing after the event with external or related online resources/references.
Welcome to Webinar #2!

Today’s Agenda:

• Oxitec’s Scientific Publications, Independent Validation and Data Transparency
• Recent Community Engagement & Chance to Join the Project!
• Your Questions, Answered

Documentation, resources, references, and other information are available at oxitec.com/california
Invasive *Aedes aegypti*, pyrethroid resistance, and challenges unique to *Aedes aegypti*

- Potential risk of local dengue, Zika, chikungunya, and yellow fever transmission.
- 2013: *Ae. aegypti* detected in Fresno, Madera, and San Mateo Counties.
- 2014: *Ae. aegypti* persisted in those 3 counties and were also detected in Kern, Tulare, Los Angeles, and San Diego Counties.
- 2015: Detected in Imperial and Orange Counties.
- Inherent challenges to *Ae. aegypti* control. Cryptic harborages, oviposition & larval sites, daytime behavior.
- Insecticide resistance: Need more tools in our toolbox.
Ten Districts in California Expressed Interest

- Each expressed an **interest to participate on pilot projects**.
- Their names were formally submitted in our initial EUP amendment to the EPA, later narrowing this down to Tulare, Stanislaus, Fresno and San Bernardino counties.
- Some counties/districts have had abundant populations of *Aedes aegypti* since 2013-2014.
- Others detected this invasive pest as recently as 2020.
Oxitec’s Scientific Publications, Independent Validation and Data Transparency
Oxitec male mosquitoes mate with invasive female pests, and only the male offspring of these encounters survive.

- **Targeted Suppression**
- **Safe, Non-Toxic, Non-Allergenic**
- **Proven Effective**
- **Male-Only Releases** (male mosquitoes do not bite!)
- **Traceable in the Field**
- **Self-Limiting in the Environment**

**Self-limiting gene**

**Marker gene**
Oxitec’s Technology: Over 100 Scientific Peer-Reviewed Articles

https://www.oxitec.com/en/our-technology#publications
Peer Review and the Scientific Method

Diagram adapted from https://authorservices.wiley.com/Reviewers/journal-reviewers/what-is-peer-review/the-peer-review-process.html
**Who Are Peer Reviewers?**

- Scientific experts in the field
- Proven scientific record
- Selected by journals following a rigorous process
- Independent – No competing interests
- Anonymous
- No remuneration

**What Do They Judge?**

- Novelty and originality
- Topicality and relevance
- Scientific integrity (study design, data collection and analysis)
- Consistency (results vs conclusions)
- Language, style and use of references
- Ethical standards
Peer-Reviewed: Development In Multiple Mosquito Species

**BMC Biology**

**Late-acting dominant lethal genetic systems and mosquito control**

Hoang Kim Phuc1, Morten H Andersen1, Rosemary S Burton1, Céline Vass1, Matthew J Epton1, Gavin Pape1, Guoliang Fu2, Kirsty C Condon1,2, Sarah Scaife2, Christl A Donnelly3, Paul G Coleman3,4, Helen White-Cooper1, and Luke Alphley*1,2

**DsRed2 transient expression in Culex quinquefasciatus mosquitoes**

André Barretto Bruno Wilke1,2, Sarah Scaife2, Luke Alphley2,3, Mauro Toledo Marrelli1

Culex quinquefasciatus mosquitoes have been successfully genetically modified only once, despite the efforts

**Female-Specific Flightless (fsRIDL) Phenotype for Control of Aedes albopictus**

Geneviève M. C. Labbé1,2, Sarah Scaife1, Siân A. Morgan1, Zoë H. Curtis1, Luke Alphley1,2,3

1Division of Biology, Imperial College London, Silwood Park, Ascot, United Kingdom; 2Department of Zoology, University of Oxford, Oxford, United Kingdom; 3Department of Biological Sciences, Section of Genetics and Molecular Biology, University of Naples “Federico II”, Naples, Italy

**Development of a population suppression strain of the human malaria vector mosquito, Anopheles stephensi**

Oswaldo Mariniotti1, Nipole Jasinskiene1, Aniko Fazekas1, Sarah Scaife2, Guoliang Fu2, Stefanie T Mattingly1, Karissa Chow1, David M Brown3, Luke Alphley2,4 and Anthony A James1,2

1Institute of Inorganic Chemistry, University of Vienna, Austria; 2Centre for Infection and Immunity, School of Medicine, University of Liverpool, Liverpool, UK; 3School of Life Sciences, University of Manchester, Manchester, UK; 4Department of Zoology, University of Oxford, Oxford, UK
Full independent evaluation and assessments demonstrate potential of the technology for control of:

- Aedes aegypti
- Aedes albopictus
- Culex quinquefasciatus
- Anopheles stephensi

Application to a range of disease vectors

Oxitec mosquitoes offer advantages

Minimal effect on fitness
Peer Reviewed: Full Biosafety of Oxitec Insects

**BMC Biology**

Research article

Late-acting dominant lethal genetic systems and mosquito control

**Scientific Reports**

Exposure to genetically engineered olive fly (Bactrocera oleae) has no negative impact on three non-target organisms
Theo Maroulis, Clare Cassidy, Esther Milli, Martha Kousidou, Enca Martin-Rendon, Simon Warner, Augusto Louz & Camila Borch
Full independent evaluation and assessments demonstrate:

- No impact on non-target organisms
- No evidence of niche replacement
- No long-term persistence of the self-limiting gene
- Biology comparable to wild-type counterparts

Non-toxic and non-allergenic

Rapidly disappears from the environment

Insecticide susceptible
Peer-Reviewed: Field Performance of Oxitec Mosquitoes
Peer-Reviewed: Field Performance of Oxitec Mosquitoes

<table>
<thead>
<tr>
<th>STRAIN</th>
<th>COUNTRY</th>
<th>LOCATION</th>
<th>YEAR</th>
<th>INDEPENDENT SCIENTIFIC REVIEW</th>
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<tbody>
<tr>
<td><strong>1st Gen (OX513A)</strong></td>
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<td>Brazil</td>
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<td>Pedra Branca</td>
<td>2013-2015</td>
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<td><strong>2nd Gen (OX5034)</strong></td>
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<tr>
<td>Brazil</td>
<td>Indaiatuba – adult release</td>
<td>2018-2019</td>
<td>Publication expected later in 2022</td>
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<td>USA</td>
<td>Florida Keys – egg release</td>
<td>2021-</td>
<td>Project ongoing</td>
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Peer-Reviewed: Development In Agricultural Pests


The research highlights the development of a genetically engineered pest insect that is self-limiting, focusing on its potential for future crop protection.

Gene editing of field-cage populations of Mediterranean fruit flies

This study explores the gene editing of Mediterranean fruit flies, aiming to control their populations effectively.

Control of the olive fruit fly using genetics-enhanced sterile insect technique

The focus is on using genetics to enhance sterile insect techniques for controlling the olive fruit fly.
Full independent evaluation and assessments demonstrate technical development in agricultural pests:

- Fall armyworm
- Mediterranean fruit fly (fruit)
- Pink bollworm (cotton)
- Diamondback moth (field crops)
- Olive fly (olives)

Promising and sustainable crop protection

Strong field performance

Dilution of insecticide resistance
Oxitec’s Technology: Reviewed By Independent Regulators
Overview of EPA’s Scientific Assessment and Approval

Key Elements:
- 14-month in-depth process
- Exhaustive scientific review
- Risk assessment
- Multi-agency support
- Public comment & responses

By the Numbers:
- 70+ documents submitted
- 25 commissioned studies
- 4,500+ pages, including 2,500+ pages of scientific peer-reviewed literature

Data Requirements Fulfilled by Oxitec (partial list)

Environmental Assessments:
- Fish
- Birds
- Mammals
- Plants
- Aquatic Invertebrates
- Insects
- Endangered Species

Health Assessments:
- Trait Penetrance
- Oral Toxicity
- Inhalation Toxicity
- Ocular Toxicity
- Dermal Toxicity
- Allergenicity
- Vector Competence

Mosquito Characterization and Performance:
- Insecticide Susceptibility
- Trait Penetrance
- Tetracycline Response
- Stability of Genetic Traits
- Trait Persistence
- Field Data (Brazil)

- Protein Stability
- Arbovirus Screening
- Introgression Analysis
- Complete SOPs
- Analytical Methodologies
EPA Conclusion: Oxitec Mosquitoes are Safe for Humans, Wildlife, and the Environment

Independently validated: no effects on endangered species or critical habitat, whether direct or indirect.

SAFE FOR

- Fish
- Birds
- Mammals
- Plants
- Invertebrates
- Other aquatic animals

- For example, third-party independent labs found that freshwater fish and invertebrates consuming a diet of 70% OX5034 mosquito larvae fared no differently to fish and invertebrates fed 70% non-Oxitec mosquito larvae.

‘OX5034 male mosquitoes do not bite people or wildlife’
Regulating Oxitec Mosquitoes in the US

Dossiers:
- Environmental Impact
- Human Health
- Feeding Studies
- Technical Data
- Operating Procedures

Oxitec mosquitoes regulated as a ‘biopesticide’ by EPA

Protocols, metrics, and analysis are predetermined by EPA

Wolbachia mosquitoes are regulated under the same rules

Federal EUP
- Dossier
- Scientific literature
- External experts

State EUP/RA
- Dossier
- EPA risk assessments
- Scientific literature

Local Oversight
- Project planning
- Board approval

Federal Product Registration
- Dossier
- EUP field data
- International data
Oxitec’s *Aedes aegypti* mosquitoes evaluated by an independent body of 27 academic experts that comprise Brazil’s regulator CTNBio.

**National Biosafety Approval in Brazil**

2020 – Oxitec mosquitoes receive full biosafety approval

- Free to release anywhere without license or restriction.
- Over 20 million released protecting thousands of people without any adverse effect.
- Available for sale commercially ([aedesdobem.com.br](http://aedesdobem.com.br)).
World-Class Partners, Collaborators and Regulatory Record

Select Partners and Underwriters

Select Current and Historical Collaborators

Positive Regulatory Approvals and Opinions
Florida Keys 2021 Results Overview

Key Performance Outcomes

- Oxitec’s self-limiting gene maintains effectiveness in the field
- Dose rates are suitable for use
- Oxitec males performed excellently
- Box dosing established effective overflooding against invasive species
- Oxitec males mated successfully
- Oxitec progeny accessed cryptic breeding sites (this is good)
- No females released
Independent Validation of Planned Project in Visalia

- Delta MVCD
- Independent Advisory Group
- California State Regulators
- Federal Regulators
Get Involved

oxitec.com/california

Proyecto Delta MVCD – Oxitec Para el Control de Mosquitos

Oxitec has received the federal approval necessary to carry out a pilot project in the Tulare county, with the aim of evaluating the effectiveness of the mosquito mating technique. The official order for the project pilot is pending.

Oxitec is committed to communicating with the residents of Tulare county, and to listening to them. Please take a moment to share your preferences of communication with us by completing this brief questionnaire.

Complete the questionnaire visiting: oxitec.com/california

The Delta Mosquito and Vector Control District (Delta MVCD) has invited Oxitec to collaborate on a field project in Visalia, California. If approved by state regulators, the Delta MVCD and Oxitec will evaluate the effectiveness of Oxitec’s non-biting male mosquitoes to control the invasive, disease-spreading Aedes aegypti mosquito in the field.

Join our Delta MVCD - Oxitec Mosquito Project!

What is your name?*

How would you like to be involved?*

I would like to host a box

I would like host a trap

Submit

oxitec.com/california

1st Delta MVCD-Oxitec Public Educational Webinar, April 26th, 2022

An introduction to Oxitec in California looks ahead to strong partnerships with local governments, communities, and experts

Please visit oxitec.com/california for additional resources.
We Will Run a Series of Ten Interactive and Educational Webinars

- An Introduction to Oxitec in California: A Project Based on Strong Partnerships with Local Governments, Communities and Experts
- Oxitec’s Scientific Publications, Independent Validation, and Data Transparency
3. Oxitec in California: Community Engagement, Participation, and Consultation by Delta MVCD and Oxitec
4. Oxitec’s Technology Part 1: How It Works and Why It Was Made to Empower Local Communities
5. Oxitec Technology Part 2: History, Partnerships, and a Decade of Results Around the World
6. California, Mosquitoes and Climate Change: Why Oxitec Was Invited to California and the Urgent Need for Innovative Pest Control Technologies
7. Oxitec in California: Piloting Oxitec’s Friendly™ Mosquitoes in Partnership with the Delta MVCD
8. Oxitec’s Technology and Sustainability: Providing Effective Mosquito Control While Preserving Biodiversity, Endangered Species and Protecting Our Environment
9. Inside Oxitec: Q&As with Oxitec’s Senior Scientists and a Virtual Tour of Oxitec’s Facilities Globally
10. Independent Views: Panel Discussion with Independent Experts on Oxitec’s California Project and the Need for Sustainable Mosquito Control Technologies
Any and all questions on this evening’s topics are welcome!

(If we run out of time tonight, email info@oxitec.com and we will attempt to answer your question if it isn’t included in the growing FAQ or post-event summary we publish online at oxitec.com/california and deltamvcd.org)
THANK YOU!

A summary of this event, as well as more Q&As, resources, facts, and background materials will be made available at oxitec.com/california