Oxitec Mosquito Vector Control Technology

A New Paradigm to combat Dengue, chikungunya and the emerging threat of Zika
Mosquitoes – The World’s Deadliest Animal

The World's Deadliest Animals
Number of people killed by animals per year

- Mosquito: 725,000
- Human: 475,000
- Snake: 50,000
- Dog: 25,000
- Tsetse fly (sleeping sickness): 10,000
- Assassin bug (Chagas disease): 10,000
- Freshwater snail (Schistosomiasis): 10

Source: GatesNotes
The Impact of Zika on the Health System, the Environment, National Economy, and International Travel Is Growing
March 2016 research article regarding Zika virus pandemic

### Travel related Zica cases in USA

<table>
<thead>
<tr>
<th></th>
<th>Travel related</th>
<th>Local transmission</th>
<th>Pregnant</th>
<th>Guillain-Barré</th>
</tr>
</thead>
<tbody>
<tr>
<td>US mainland</td>
<td>388</td>
<td></td>
<td>33</td>
<td>1</td>
</tr>
<tr>
<td>Florida:</td>
<td>84</td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Territories</td>
<td>3</td>
<td>500</td>
<td>48</td>
<td>4</td>
</tr>
</tbody>
</table>

**CDC 20th April 2016**

Governor Scott directed the State Surgeon General to issue a Declaration of Public Health Emergency for the counties of residents with travel-associated cases of Zika.

The Declaration currently includes the 15 affected counties:

- Alachua
- Hillsborough
- Palm Beach
- Brevard
- Lee
- Polk
- Broward
- Miami-Dade
- Santa Rosa
- Clay
- Orange
- Collier
- Osceola
- Seminole
- St. Johns
The Current Insecticide Model for Mosquito Vector Control

Challenges
+ Inadequate control
+ Insecticide resistance
+ Public concerns about health effects and impacts on the environment and other species

Example of Mosquito Eradication in a School Room
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002/4</td>
<td>Company formed as spin out from Oxford University Technology platform developed and exemplified in both agricultural and mosquito species</td>
<td>Global first release of a GE insect Pink Bollworm (marker only) in USA Mosquito development spurred by Gates funding</td>
</tr>
<tr>
<td>2005/7</td>
<td>First outdoor release of OX513A mosquito in the Caymans</td>
<td>Environmental Impact Statement in the USA – environmentally preferred solution</td>
</tr>
<tr>
<td>2008/9</td>
<td>First agricultural collaborations</td>
<td>Oxitec Brazil established</td>
</tr>
<tr>
<td>2010/12</td>
<td>First larger scale urban project starts in Jacobina, Brazil</td>
<td>USDA approval for agriculture trial in USA</td>
</tr>
<tr>
<td>2013</td>
<td>Oxithec Brazil National Biosafety approval in Brazil</td>
<td>Brazil approval for agricultural trial</td>
</tr>
<tr>
<td>2014</td>
<td>WHO VCAG recommendation for large scale</td>
<td>First direct projects OX513A Brazil</td>
</tr>
<tr>
<td>2015</td>
<td>First agricultural strains into development Medfly, DBM &amp; Olive fly</td>
<td>Oxitec acquired by Intrexon to accelerate development</td>
</tr>
</tbody>
</table>
How Oxitec’s Technology Works

Inject genes into insect egg

Self Limiting Gene

+ Inherited and offspring do not survive to adulthood
+ Repressed with an antidote during male insect production, allowing low cost multiplication
+ After releases stop, genes do not persist in the environment

Fluorescent Marker Gene

+ Fluorescent protein detected by special light
+ Monitoring of pest population suppression
+ Releases adjusted in nearly real time
+ ‘Track and trace’ capability

Oxitec male mosquitoes are produced for release and mate with pest females

Offspring die before they can reproduce and transmit disease
Key Benefits

Efficiency
- Targeted delivery: males are attracted to wild females whose offspring die at the larvae and pupal stage (consuming resources along the way)
- Insects and offspring contain a marker gene that is easy to monitor - “track and trace”
- Local deployment by local people

Safety
- Male-only releases (only female mosquitoes bite)
- Genetic change is not toxic or allergenic

Environment
- Species-specific pest control, no off-target effects
- Reduction of Aedes does not impact insects or other animals that may feed on Aedes
- Neither insects nor progeny persist over time in the environment
Promising Suppression Results Ongoing in Piracicaba, Brazil

Reduction in wild mosquito larvae by 82%

- Oxitec and Piracicaba City Hall are expanding the ‘Friendly Aedes aegypti Project’ in Piracicaba, Brazil
- Oxitec is planning a new mosquito production facility in Piracicaba
Oxitec Mosquito Trial Results Summary

Up to 90+% suppression of *Aedes aegypti* in selected field trials and projects

- **Cayman Islands**: 96%
- **Pedra Branca**: 92%
- **Itaberaba**: 93%
- **Mandacaru**: 99%
- **Panama**: 93%

**Cayman**: Mosquito Research Control Unit
**Brazil**: University of São Paulo and Moscamed
**Panama**: The Gorgas Institute
**Attacking Global Epidemics at the Source: Brazil Case Study**

**Early 1970s**
- No Aedes aegypti
- No dengue

**Recent years**
- 1.5 million cases of dengue in 2015, up 176% y-o-y with 811 dengue-related deaths
- First local transmission of chikungunya in 2014 and Zika virus entered in 2015
- Over $1 billion spent on the dengue vector control program annually

**Oxitec in Brazil – 2011 to Present**
- Trials 2011–13
- National Biosafety Approval granted 2014
- Oxitec do Brasil established
- In April 2015, Piracicaba became world’s first municipality to release Oxitec mosquitoes operationally – project now being expanded

96% of local Piracicaba residents support the Oxitec program

Brazil press describe Oxitec solution as *Aedes aegypti* do bem: ‘the good mosquito’
A New York woman caught dengue while vacationing in Key West. The first case of dengue in the area since 1933. Dengue was transmitted to an additional eighty-seven people in the area between ‘09 and ‘10.

The Key West Mosquito Control District contacts Oxitec to explore new solutions to control the Aedes Aegypti mosquito.

Oxitec applies to the Food & Drug Administration for permits to hold a field study in Key West, Fla.

Key West proposes using Oxitec genetically modified mosquito to stop the Aedes Aegypti mosquito.

The Food & Drug Administration issues a finding of “No Significant Environmental Impact” from a proposed field study.
Rigorous evaluation by independent experts

- Detailed regulatory dossiers submitted and approved in multiple countries

- National Biosafety Commission in Brazil approved Brazil-wide use in April 2014

- FDA-CVM publication of preliminary EA with FONSI March 2016

- WHO recommendation for OX513A March 2016
Strong Consumer Support

Piracicaba, Brazil

Florida, USA

+ Pre-zika outbreak surveys above show strong support
+ Post-zika Purdue study 78% support in USA*

Production and Release
More than 130 million Oxitec mosquitoes released worldwide
Global Supply Vision

Global facilities produce eggs—highly durable and can ship globally.

Regional and local facilities prepare pupae and distribute.
Summary

+ Oxitec now wholly-owned by Intrexon, a U.S. company with the expertise, scale, and determination to execute on significant global issues

+ Oxitec has had field success supressing the pest populations of *Aedes aegypti* of up to 90+% 

+ Current results have proven entomological end points

+ CTNBio in Brazil have approved the Oxitec mosquito (OX513A) from an efficacy and environmental safety perspective for commercial application

+ FDA-CVM have issued a preliminary Finding of No Significant Impact

+ WHO have made a recommendation for pilot deployment

+ Oxitec has solutions that apply to *Aedes albopictus* as well

+ The technology is compatible with current interventions and would be synergistic with future vaccine and therapeutic drug interventions
QUESTIONS?