



COMMENTS OF REASON FOUNDATION ON THE PROPOSED PESTICIDE
EXPERIMENTAL USE PERMITS; APPLICATIONS: OXITEC LTD., U.S. Environmental
Protection Agency. Docket ID No. [EPA-HQ-OPP-2017-0756] March 15, 2018

Thank you for the opportunity to submit this comment regarding the request by Oxitec Ltd. for an experimental use permit (EUP) for the OX513A *Aedes aegypti* mosquitoes. This comments is being submitted on behalf of Reason Foundation.

Reason Foundation's nonpartisan public policy research promotes choice, competition and a dynamic market economy as the foundation for human dignity and progress. Reason produces rigorous, peer reviewed research and directly engages the policy process seeking strategies that emphasize cooperation, flexibility, local knowledge, transparency, accountability and results.

The main focus of this submission is the costs and benefits associated with the issuance of the EUP requested by Oxitec Ltd. to test the OX513A *Aedes aegypti* mosquitoes expressing tTAV protein in the states of Florida and Texas, and the possible wider impacts of approving the EUP to evaluate the efficacy of OX513A mosquitoes as a tool for suppression of wild *Aedes aegypti* mosquito populations.

1. *Aedes aegypti* mosquitoes are the leading cause of several deadly diseases, including dengue, yellow fever, chikungunya, and Zika.

Mosquitoes are one of the deadliest animals in the world. 80% of the world's population is at risk of one or more vector-borne diseases, according to the World Health Organization. Their ability to carry and spread diseases to humans causes millions of deaths every year. *Aedes aegypti* is one of the most widespread mosquito species globally and responsible for a number of serious viral diseases, including the following:

- Yellow fever – Endemic in 47 countries in Africa and Latin America. Mortality rate among severe cases of the disease is estimated at 20 to 50%. While the number of cases in those countries declined for past 10 years due to a global vaccine initiative begun in

5737 Mesmer Avenue, Los Angeles, CA 90230-6316 · 310-391-2245 · Fax: 310-391-4395 · www.reason.org

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2006, outbreaks have been recently reported in Brazil and several African countries. (<http://www.who.int/mediacentre/factsheets/fs100/en/>)

- Dengue – The worldwide incidence of dengue has risen 30-fold in the past 30 years, and more countries are reporting their first outbreaks of the disease. According to the World Health Organization, dengue is endemic in more than 128 countries, with 3.9 billion people at risk. Estimates indicate that 390 million are infected with dengue every year. The actual numbers of dengue cases are underreported and many cases are misclassified. (<http://www.who.int/mediacentre/factsheets/fs117/en/>)
- Chikungunya – Has been identified in 60 countries in Asia, Africa, Europe and the Americas. (<http://www.who.int/mediacentre/factsheets/fs327/en/>)
- Zika virus disease – Zika virus is known to circulate in Africa, the Americas, Asia and the Pacific. Both the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (CDC) have confirmed that Zika virus is a cause of microcephaly and other severe fetal brain defects.¹ In 2017, 84 countries, territories or subnational areas reported evidence of vector-borne Zika transmission. (<http://www.who.int/mediacentre/factsheets/zika/en/>)

Aedes aegypti is also a potential vector of Venezuelan Equine Encephalitis virus.²

2. Distribution of *Aedes aegypti* in the United States.

The geographical reach of the *Aedes aegypti* species is not limited to the equatorial regions. CDC estimates for *Aedes aegypti* geographical range put at risk almost the entire Southern half of the U.S. (see Figure 1).

- Dengue- The last reported dengue outbreak in the continental US was in south Texas in 2005. However, most dengue cases in U.S. citizens occur in Puerto Rico, the U.S. Virgin Islands, Samoa and Guam, which are endemic for the virus and outbreaks follow a seasonal pattern.³
- Chikungunya- Prior to 2006, chikungunya virus disease was rarely identified in U.S. travelers. Since 2006, studies identified an average of 28 people per year in the U.S. with positive tests for recent chikungunya virus infection (Range 5–65 per year), including locally transmitted cases in Florida, Puerto Rico, and the U.S. Virgin Islands.⁴

¹ <http://www.cdc.gov/media/releases/2016/s0413-zika-microcephaly.html> and <http://www.cdc.gov/media/releases/2016/s0413-zika-microcephaly.html>

² Larsen JR, Ashley RF. Demonstration of Venezuelan equine encephalomyelitis virus in tissues of *Aedes Aegypti*. *Am J Trop Med Hyg.* 1971 Sep; 20(5):754-60.

³ <https://www.cdc.gov/dengue/epidemiology/index.html>

⁴ <https://www.cdc.gov/chikungunya/geo/united-states.html>

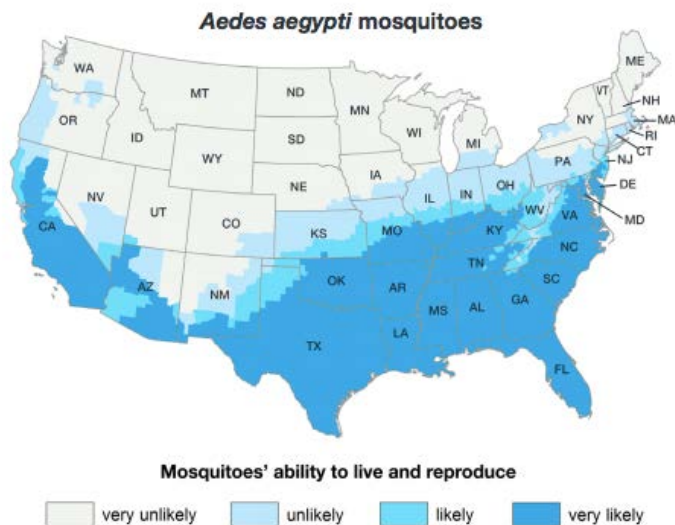


Figure 1: <https://www.cdc.gov/zika/pdfs/zika-mosquito-maps.pdf>

- Zika virus disease- Several areas in the United States have the *Aedes aegypti* mosquitoes that can become infected with and spread Zika, chikungunya, and dengue viruses. Recent outbreaks in the United States of chikungunya and dengue have been relatively small and limited to a small area. Areas with past outbreaks of chikungunya and dengue are considered at higher risk for Zika. These include U.S. territories like Puerto Rico, the U.S. Virgin Islands, and Guam. Local outbreaks have also been reported in parts of Hawaii, Florida, and Texas.⁵

In 2017, 433 cases of Zika virus disease cases were reported in the 50 states, including 5 cases acquired through local mosquito-borne transmission in Florida and Texas. Almost 654 locally-acquired infections occurred in U.S. territories.⁶ Since January 1, 2018, 10 Zika virus disease cases have been reported in the U.S.⁷

3. Current *Aedes aegypti* control methods are not working and are costly.

Currently, prevention and control of dengue fever, Zika virus disease, and chikungunya in the U.S. depend solely upon widespread implementation of effective mosquito control measures, because vaccines and effective anti-viral therapies for these diseases are not yet available.

⁵ <https://www.cdc.gov/zika/vector/range.html>

⁶ <https://www.cdc.gov/zika/reporting/2017-case-counts.html>

⁷ <https://www.cdc.gov/zika/reporting/2018-case-counts.html>

Existent techniques (e.g. insecticides and breeding site management) have repeatedly proven inefficient,⁸ costly, and sometimes even toxic. The repeated use of chemical insecticides is leading to rising resistance worldwide creating challenges for mosquito control programs.⁹ In Texas, the U.S. Air Force was mobilized after Hurricane Harvey to spray 6 million acres with naled, an organophosphate pesticide. The Florida Keys Mosquito Control District spends about \$1.1 million per year in the Key West area to achieve an estimated 50% reduction of the *Aedes aegypti* population.¹⁰

4. OX513A: technology and potential benefits.

Oxitec's mosquito, OX513A, is a self-limiting strain of the *Aedes aegypti* male mosquito, which does not bite or transmit diseases (it is only the female *Aedes aegypti* mosquito that transmits diseases). Released to mate with wild females, the offspring inherit a self-limiting gene and die before becoming functional adults, thereby reducing the wild population. The self-limiting gene, tTAV (tetracycline repressible transactivator variant), is a gene variant that has been optimized to only work in insect cells. In the wild, offspring that contain the self-limiting gene make a non-toxic protein that ties up the cell's machinery so its other genes are not expressed and the insect dies. The proteins produced are non-toxic in the insects, so if any animals eat them it would be the same as eating a wild insect – they are digested in just the same way that all other insects are digested.

The technology has undergone successful trials since 2009 in several countries (including Brazil, Panama, Malaysia, and the Cayman Islands), establishing the validity of the Oxitec approach: the size of the *Aedes aegypti* population in the targeted areas decreased by more than 90%.

Currently, OX513A has regulatory approvals for import and contained testing in Brazil, Cayman Islands, France, India, Malaysia, Singapore, Thailand, Vietnam.

The U.S. Food and Drug Administration (FDA) has already acknowledged the importance and potential benefits of using OX513A when it published its final assessment documents (a final environmental assessment (EA) and finding of no significant impact (FONSI)) in August 2016. The FONSI statement corroborated the EA's conclusion that the proposed field trial will not have a significant impact on the environment.

We encourage EPA to take these positive acknowledgments into consideration when deciding on the course of Oxitec's request to test the OX513A *Aedes aegypti* mosquitoes.

⁸ Yakob L, Walker T. Alternative vector control methods to manage the Zika virus outbreak: More haste, less speed - Authors' reply. *Lancet Global Health*. 2016;4(6):e365-6 10.1016/S2214-109X(16)00086-3

⁹ Ranson, H., Burhani, J., Lumjuan, N., & Black IV, W. C. (2010). Insecticide resistance in dengue vectors. *TropIKA. net*, 1(1), 1-12.

¹⁰ <http://keysmosquito.org/oxitec-ox513a-trial/>

5. Summary and recommendation.

When evaluating the costs and benefits of issuing an EUP for Oxitec's OX513A *Aedes aegypti* mosquito, we ask EPA to carefully consider these points:

- The burden associated with *Aedes aegypti* transmitted diseases is very high, including widespread loss of human life. The U.S. is not excluded from this burden.
- The risks of delaying experimental use of OX513A are potentially enormous. The inefficiency of current mosquito control methods combined with the geographical spread of the *Aedes aegypti* species means millions of people will continue to get sick unnecessarily if the implementation of more efficient technologies is delayed.
- Oxitec's OX513A mosquitoes represents significant progress in the control of vector-borne diseases. Successful field trials indicate the validity of using OX513A and suggest that it is ready to be scaled up.
- The evidence indicates that there is unlikely to be any significant adverse impact on the environment or human health. To the contrary, the reduction in use of pesticides is likely to benefit the environment, while the greater efficacy and efficiency of this mosquito control method is likely to benefit human health.
- Further field trials, including those proposed in the EUP application will help better evaluate the effects of OX513A on the environment and human health.
- EPA's EUP approval does not mean that Oxitec's OX513A mosquitos are approved for commercial use.

Given current inefficient mosquito-control methods, the high burden of vector-borne diseases, and the positive results of previous field trials of the OX513A *Aedes aegypti* mosquito, Reason Foundation urges the EPA to move forward as quickly as possible in approving Oxitec's request for an EUP to undertake field trials in Florida and Texas. Unfounded fears about this safe technology should not prevent it being implemented as part of the solution to a serious health problem.

Thank you for your time and consideration of these comments.

Sincerely,

Krisztina Pusok
Research Associate
Reason Foundation

Julian Morris
Vice President of Research
Reason Foundation