

Frequently Asked Questions About Oxitec's Friendly™ *Aedes aegypti* Mosquitoes

What is a self-limiting mosquito?

Oxitec's Friendly[™] non-biting male *Aedes aegypti* mosquitoes carry a self-limiting gene that prevents female offspring from surviving, allowing for male-only production. After Friendly[™] *Aedes aegypti* male mosquitoes are released and mate with invasive female mosquitoes, the number of disease-transmitting female *Aedes aegypti* is reduced. Only female mosquitoes bite and are capable of transmitting diseases, which is why they are targeted. Oxitec's mosquitoes also have a fluorescent marker gene which enables them to be distinguished from invasive mosquitoes for effective monitoring.

Why target the Aedes aegypti mosquito?

Oxitec's non-biting male Friendly[™] *Aedes aegypti* mosquitoes carry a self-limiting gene that prevents their female offspring from surviving, allowing for male-only production. After Friendly[™] male mosquitoes are released and mate with invasive pest females, the number of female *Aedes aegypti*, which are capable of transmitting viruses, is reduced.

We don't have a Zika or dengue outbreak in California. Why do we need self-limiting mosquitoes to control invasive *Aedes*?

The COVID pandemic has reinforced the need for proactive public health interventions before there is a wide-spread disease outbreak. Since first being detected in 2013 in the Central Valley, *Aedes aegypti* mosquitoes have spread to more than 300 towns and cities throughout California increasing the risk of transmission of viruses that cause dengue, chikungunya, Zika, and yellow fever. According to the <u>California Department of Public Health</u>, "none of these viruses are currently known to be transmitted within California, but thousands of people are infected with these viruses in other parts of the world, including in Mexico, Central and South America, the Caribbean, and Asia. The presence of *Aedes aegypti* mosquitoes in California poses a threat that Zika, dengue, and chikungunya viruses can be transmitted in infested areas from returned infected travelers."

Where else have you released these mosquitoes?

Oxitec recently secured regulatory approvals from the US Environmental Protection Agency (EPA) and the Florida Department of Agriculture and Consumer Services (FDACS) to release Friendly[™] Aedes aegypti mosquitoes in the Florida Keys. The decisions included input from the CDC and seven other State of Florida agencies, including the Departments of Health and Environmental Protection. These releases began in April 2021.

In 2019, Oxitec released Friendly[™] *Aedes aegypti* mosquitoes in São Paulo State in Brazil and after 13 weeks the technology suppressed up to 95% of *Aedes aegypti*. This showed the potential to reduce the risk of disease-transmission by this pernicious vector of dengue, Zika, chikungunya and yellow fever. Together these viruses infect hundreds of thousands of Brazilians every year, with devastating consequences.

In May 2020, Oxitec received full biosafety approval for this technology from Brazil's national biosafety regulatory authority CTNBio after demonstrating the technology's full safety to human health and the environment. Independent research found community support for the project was overwhelmingly high, with 94% of residents supporting the use of Oxitec's mosquito technology in their neighborhoods.

Why are innovative control techniques needed in California?

Traditional approaches have been providing a valuable defense against mosquito-borne diseases for decades and will continue to do so. However, the geographical range of this invasive species is increasing, and *Aedes aegypti* seeks harborage and lays eggs close to people's homes. This makes it very time intensive to target with applications of larvicides. In addition, this species has become resistant to some pyrethroids, the most commonly used class of mosquito adulticide. Due to the risk posed by this particular species of mosquito, public health and mosquito experts need new methods to control *Aedes aegypti* mosquitoes in order to protect public health.

Do Oxitec's Friendly™ Aedes aegypti mosquitoes bite?

No, like all male mosquitoes, Oxitec's mosquitoes do not bite. Male mosquitoes lack the mouthparts to bite and only female mosquitoes bite and are capable of transmitting diseases.

What are the risks if a female Oxitec mosquito bites someone?

Zero - there will be no Oxitec female mosquitoes and thus no risk. Only male mosquitoes are released because the self-limiting gene prevents females from surviving in the pre-release production stage. Oxitec Friendly^M Aedes aegypti male mosquitoes are safe, non-toxic, and non-allergenic.

How long do the sterile male Oxitec mosquitoes live for?

As adults, male Oxitec *Aedes aegypti* live for just few days in the wild and usually do not survive for more than a week. This is similar to wild male mosquitoes. Wild female *Aedes aegypti* tend to live a little longer, up to several weeks.

Why do only the female offspring die?

Oxitec's Friendly *Aedes aegypti* carry a self-limiting gene that is only active in females, which prevents females from surviving. Males are not affected by this gene, so they can survive as normal. Female mosquitoes bite and are capable of transmitting diseases which is why they are targeted with the self-limiting gene.

Are self-limiting gene mosquitoes an environmentally sustainable control tool?

Yes. The <u>International Plant Protection Convention</u>, an intergovernmental treaty signed by over 180 countries aiming to protect the world's plant resources from the spread and introduction of pests, categorizes sterile insects as beneficial organisms. According to the <u>International Atomic Energy Agency</u>, "Sterile insects are not self-replicating and therefore cannot become established in the environment. Breaking the pest's reproductive cycle, also called autocidal control, is by definition species-specific. The SIT does not introduce non-native species into an ecosystem."



Will Oxitec mosquitoes harm birds, bees, bats, fish, turtles, or other wildlife?

No. Self-limiting mosquitoes work by finding and mating with invasive *Aedes aegypti* females and the suppression effect is specifically targeted to this species of mosquito. This specificity leaves non-target species, such as bees, butterflies and other wildlife, unharmed.

Will Oxitec's technology replace insecticides and other control measures?

No. Insecticides are a valuable option available to mosquito control agencies but in some situations, they have increasing limitations as some mosquito species have become resistant to commonly used insecticides. Mosquito and vector control agencies in California use an Integrated Vector Management approach that relies on a suite of management options to optimize protection against disease-carrying mosquitoes and maximize sustainability. Oxitec Friendly™ *Aedes aegypti* mosquitoes are intended to be one part of this Integrated Vector Management approach.

What is the process and timeline for securing approval for the pilot projects in California?

Oxitec has submitted an amendment to the U.S. Environmental Protection Agency for an Experimental Use Permit (EUP) to implement pilot projects in selected counties in California. As part of this application process, the public will have an opportunity to submit comments to the EPA. The EPA will review and respond to the comments before issuing a final decision, which is anticipated in late 2021. If the EPA approves Oxitec's amendment, the company will need to secure approval from the California Department of Pesticide Regulation, and any necessary local approvals before initiating pilot projects.

What does the EPA's review entail?

The Environmental Protection Agency's scientific and environmental assessments for the original Experimental Use Permit included a review of over 4,500 pages of data and protocols, including 2,500+ pages of scientific peer-reviewed literature. The exhaustive scientific review and risk assessment spanned 14 months and involved a robust process to incorporate public input and respond to comments. In addition to the original EUP reviews, which provided a comprehensive risk assessment of potential risks to humans and the environment, the EPA is expected to carry out location-specific environmental risk assessments for the selected project locations in California.

If Oxitec gets approval for pilot projects in California what would that look like?

The project would include releases of Friendly[™] *Aedes aegypti* mosquitoes at different locations within a specified area. The precise locations and scale of the studies are yet to be determined. Evaluations would involve comparisons with untreated areas. The evaluation elements would include looking at 1) male mosquito flight range, 2) efficacy of the product (i.e. percentage of larvae that express the fluorescent gene, a measure of mating success), 3) the duration of effect, and 4) percentage of the invasive population that is impacted.



Where do you plan to do the pilot projects in California ?

Ten mosquito districts throughout the state have expressed support for bringing Oxitec's technology into California. There are several layers of regulatory review and approval that must be secured at the federal, state, and local level before Oxitec can partner with local mosquito districts. As such, it has not been determined which districts will participate in a pilot project to evaluate the efficacy of Oxitec's Friendly™ *Aedes aegypti* mosquitoes in reducing the population of invasive female *Aedes aegypti* mosquitoes, which can transit diseases.

Would California residents be subjected to an unproven technology if the pilot project moves forward?

No, this technology has been released successfully in Brazil, where it received full national biosafety approval for commercial release from the federal regulatory agency, CTNBio. Prior to any pilot projects in California, the comprehensive federal scientific review and risk assessment by the US EPA would be supplemented by a confirmation of safety for Oxitec's technology in California. This includes securing approval from the California Department of Pesticide Regulation and any necessary local approvals. Oxitec is not testing on humans and this project is not introducing risk to humans, animals, or the environment, as stated by the EPA and FDA.

Do local residents support Oxitec's project in the Florida Keys?

Oxitec's technology received support in 31 of 33 Monroe County precincts in a 2016 referendum, highlighting a broad base of support. As the Florida Keys Mosquito Control District (FKMCD) and Oxitec have jointly prepared and initiated the pilot, support in the communities has remained strong. Without the active participation of local residents who are keen to help FKMCD find solutions, the project could simply not have started.