

Despite Zika threat, plan to test 'Franken-fly' remains in federal review limbo

February 22 2016, by Jenny Staletovich, Miami Herald

At the epicenter of the Zika outbreak in Latin America, Brazil and world health officials have embraced a lab-engineered "Franken-fly" as a potential weapon to control a frightening virus suspected of causing horrific birth defects in newborns.

But six years after a pioneering test run in Key West was first proposed, a plan to deploy the genetically modified bugs in the U.S. remains on indeterminate hold.

A Marathon, Fla., lab built to produce designer males that breed non-viable offspring remains shuttered while the U.S. Food and Drug Administration continues to mull over potential environmental impacts. Meanwhile, a petition to stop those trials in the tiny, upscale neighborhood of Key Haven, just outside of Key West, continues to draw signatures - more than 160,000 so far. Whether the growing concern about Zika spreading in Florida breaks a seeming stalemate remains to be seen.

An FDA spokeswoman said last week the agency has so far received no "explicit" orders to fast-track its review, even after President Barack Obama asked for \$1.8 billion to fight the virus and expand mosquito-control programs. The agency, said spokeswoman Juli Putnam, is working as "expeditiously as possible."

But in Brazil, where between 500,000 and 1.5 million people are believed to have been infected in the last year, officials have decided

they can't afford to wait.

The *Aedes aegypti* mosquito, which carries the virus, thrives in urban tropical settings - like Brazil's many favelas. Over the eons, it has developed an insidious preference to live with humans and spread disease, that make it the "cockroach of [mosquitoes](#)," said Florida International University geneticist Matthew DeGennaro. Unlike Florida's native marsh mosquitoes, the *Aedes aegypti* evolved to be attracted to human odor.

Increasingly, government officials are looking toward what some have dubbed frankenflies for help. Last week, the World Health Organization said fogging "followed by the controlled release of [genetically modified mosquitoes](#)" is worth considering. Florida Keys Mosquito Control District executive director Michael Doyle is headed to the country later this month for a conference examining the use of sterile insects like the kind Oxitec hopes to breed in the Keys.

For the British company, the Brazilian outbreak may finally set the stage to persuade skeptical Keys residents and federal regulators.

"When chikungunya came into the Caribbean two years ago, that should have been a massive wake-up call," said CEO Haydn Perry. "We just need to get on with it."

The company has already released millions of mosquitoes in trials in Brazil and is building a production plant in the state of São Paulo. The plant, located near Piracicaba, a city of about 350,000 where 6 million mosquitoes were released last April to battle an outbreak of dengue, should be finished by mid-year. With the Zika outbreak, Perry said the company is now considering expanding it.

"The biggest question we have is, are we building (the plant) big

enough?" he said.

Florida, where 21 travel-related cases of Zika had been confirmed as of Monday, has long been at war with the *Aedes aegypti*, mostly controlling the diseases its spreads. Two years ago, chikungunya infected about a dozen Floridians and in 2009 Key West battled an outbreak of dengue - a public health threat that first prompted mosquito managers in Monroe County to ponder using the genetically modified insects in the United States.

Faced with the Zika scare, local mosquito control officials say they're keeping careful watch, but so far have no plans to change their approach even as they are getting swamped with calls.

In Miami-Dade County, which as of Monday had the most Zika cases with seven, mosquito season tends to start in late spring or early summer when marsh mosquitos, which don't carry the disease, blow in off marshes or mangroves on the coast. Despite this winter's heavy El Nino rains, mosquito populations have not risen, said Chalmers Vasquez, the county's mosquito control operations manager. The district plans to continue focusing efforts on getting homeowners, who have mostly been complaining about mosquitoes around drainage ponds and canals, to dump standing water.

"In people's minds, there's of course a reason to be concerned about it," Chalmers said. "We're trying to get the message out that canals, ditches and man-made lakes and whatever we have around here has nothing to do with this mosquito."

The Keys, with its year-round season, takes a more aggressive approach. In addition to a team of inspectors that go door to door daily in search of breeding grounds, planes routinely fog.

"What we do on day-to-day operations is what most people do in an emergency situation," said Beth Ranson, spokeswoman for the Florida Keys Mosquito Control District.

Which is what brought Oxitec to Florida, where battling mosquitoes has earned the district a reputation for cutting edge techniques.

Pitched as a safer, more affordable way of battling *Aedes aegypti*, Oxitec's engineered mosquitoes work by releasing males designed to produce offspring with a kill-switch, or defective gene that kills them. The offspring also bear a florescent marker gene so their larvae can be identified when inspectors conduct mosquito counts. That allows mosquito control districts to gauge the progress of the program.

The method was first developed to battle an outbreak of the flesh-eating screw worm - its Latin name translate to "eater of man." The nasty bug migrated from South America and by the 1930s was feasting on cattle across the Southeast, mounting up millions in losses for ranchers.

In 1953, a Texas entomologist who helped the U.S. Army develop DDT came up with the idea of sterilizing male flies with an X-ray machine. Tests conducted around the U.S., including Sanibel Island, showed huge successes. The flies are still in production in the U.S., Mexico and Panama.

What Oxitec is doing, said DeGennaro, who runs Florida International University's Mosquito Genetics and Behavior lab, is a "21st century" version of that.

Because mosquitoes can't tolerate radiation, Oxitec genetically engineered male mosquitoes, which don't bite, to be sterile and have a kill switch.

"They don't bite, they mate with as many females as they can, and then those females don't reproduce," DeGennaro said. "You're not really introducing the gene into the environment because things are dying."

Oxitec has already released about 135 million mosquitoes in different countries, Perry said, and seen wild populations of *Aedes aegypti* decline between 80 and 90 percent.

But the approach - based on a high-tech version of a decades old method - was met with bitter opposition from residents who feared technology gone wild.

"When I first heard about it, I thought it was the most advanced idea ever. Mosquito fighting mosquito," said Key West real estate agent Mila De Mier, who started the petition.

But she said she has worries the mosquitoes could cause unintended consequences and while they reduce mosquito populations, no studies link them to a reduction in disease.

"I think the technology can work, but it has to be proven it's effective," she said.

But conducting such trials, which would require thousands of participants, would be costly and time-consuming, FIU's DeGennaro said. And circumstantial evidence already exists: Researchers know when there are fewer *Aedes aegypti* buzzing around, disease drops.

He also argues that spraying is more damaging to the environment.

"When we spray, we're killing everything and that's much more upsetting to the food chain," he said.

The Brazilian outbreak also raises another troubling question: Is the virus or the mosquito that carries it changing? Until last year, Zika was an obscure disease named for a forest in Uganda with symptoms so mild health officials had trouble tracking it. Then in 2015 an outbreak began in Brazil with a new twist: about 4,000 babies were born at the same time with microcephaly that officials strongly suspect was caused by the virus. They now believe it may also be transmitted through sex, yet another wrinkle that could complicate stopping its spread.

Researchers also fear that *Aedes aegypti* could develop a resistance to insecticides. Other rapid changes are also raising concerns: warming temperatures have expanded the mosquitoes zone while global travel and urbanization of the tropics has increased.

"We've just had this huge chikungunya outbreak that spread through the Caribbean and South America. So why should we be so surprised that another mosquito-borne illness is doing the same thing?" DeGennaro said. "We have been incredibly lucky in Miami. We resisted the chikungunya outbreak. I hope we will resist the Zika outbreak."

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Citation: Despite Zika threat, plan to test 'Franken-fly' remains in federal review limbo (2016, February 22) retrieved 18 April 2024 from <https://medicalxpress.com/news/2016-02-zika-threat-franken-fly-federal-limbo.html>

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