GM Mosquito Trial Alarms Opponents, Strains Ties in Gates-Funded Project

For about a decade, scientists have debated how and when to carry out the first test release of transgenic mosquitoes designed to fight human disease—a landmark study they imagined might trigger fierce resistance from opponents of genetic engineering. A stream of papers and reports has argued that a release of any genetically modified (GM) mosquito should be preceded by years of careful groundwork, including an exhaustive public debate to win the hearts and minds of the local population.

But now, it turns out that with little public debate, a company released such mosquitoes a year ago in a fiscal paradise in the Caribbean, where they have been flying under the world's radar screen until last week. At a press conference in London on 11 November, British company Oxitec announced that it carried out the world's first small trial with transgenic Aedes aegypti mosquitoes in Grand Cayman in the fall of 2009, followed by a larger study there last summer. Oxitec chief scientist Luke Alphey also presented the unpublished resultswhich he declared a "complete success" at a meeting of the American Society of Tropical Medicine and Hygiene in Atlanta a week earlier.

The announcement has taken aback opponents of GM mosquitoes and surprised many researchers in the field of genetic control of insect vectors. And some say that staying mum was a strategic mistake that provides critics with fresh ammunition. "I don't think they did themselves a favor,"



"I would completely reject any notion that this was done secretively."

> —LUKE ALPHEY, **CHIEF SCIENTIFIC OFFICER, OXITEC**

says Bart Knols, a medical entomologist at the University of Amsterdam in the Netherlands. "This could well trigger a backlash."

Nor does the trial sit well with the collaborators in a big international project, in which Oxitec is a key member, to develop and test GM mosquitoes. The program, funded by a \$19.7 million grant from the Bill & Melinda Gates Foundation and led by Anthony James of the University of California, Irvine, has spent years preparing a study site in the Mexican state of Chiapas, where it is testing another strain of Oxitec mosquitoes in cage studies. The project, one of Gates's Grand Challenges in Global Health, would "never" release GM mosquitoes the way Oxitec has now done in Grand Cayman, says James.

Oxitec has received \$5 million from the Gates program, but the Grand Cayman trial is not part of that. "As a private company, they can push their own agenda," says James, even though this could possibly hurt

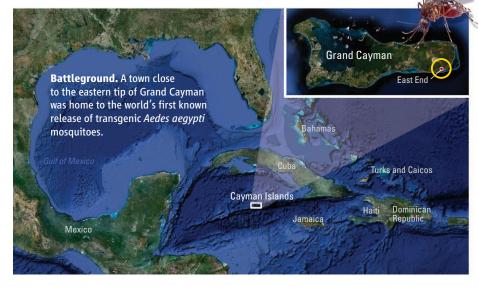
the field as a whole. "It's a

difficult situation," he says. "I would completely reject any notion that this was done secretively," says Alphey, who notes that the trial was well-known within the island's population of 50,000, "but just not picked up internationally."

Few deny that in the race to develop disease-fighting mosquitoes, Oxitec has an impressive lead. Its key idea, pioneered by Alphey while at the University of Oxford in the 1990s, is to release massive numbers of lab-bred male mosquitoes equipped with a gene that kills any offspring in the larval or pupal stage. When the males mate with females of a natural population, there are no progeny—and if the transgenic males mate more often than the natural ones, the mosquito population will dwindle or even collapse. (And because male mosquitoes don't bite, their release does not increase the risk of disease transmission to humans.)

Oxitec sees a key market in Ae. aegypti, the vector for dengue, a painful and sometimes fatal viral infection for which no drugs or vaccines exist. Many middle- and high-income countries already invest heavily in traditional mosquito-control measures to fight dengue, but the results are unimpressive—so an alternative is welcome. Alphey says the first small field study, designed to test whether the males can compete with their natural counterparts, was done on Grand Cayman in November and December of 2009. It was followed by a larger study, between May and October of this year, in which the insects' population-suppressing powers were also gauged. During that period, the team flooded about 16 hectares in the town of East End with transgenic males, about 10 for every naturally occurring wild male. By August, there were about 80% fewer mosquitoes around than in a comparable control area.

For the trial, Oxitec has worked with the Mosquito Research and Control Unit (MRCU) of the Cayman Islands, an overseas territory of the United Kingdom. The trial abided by the rules of the territory's new biosafety bill that has yet to become law, Alphey says. There were no town hall meetings or public debates because the government of the Cayman Islands didn't deem them necessary. But MRCU sent information about the study to local newspapers, Alphey says, and its 50 employees attended a lunch meeting about the project from which information filtered out to the rest of the island as well. MRCU, which could not be reached for comment, also posted a promotional video about the project on YouTube, but the clip does not mention 5





Enjoy your flight. The release of transgenic males led to an 80% reduction in the size of the local population. says Alphey.

that the mosquitoes are transgenic.

That's quite a contrast to the process the Grand Challenges project researchers used to select and prepare a site for a possible future release of Oxitec mosquitoes in Mexico. Currently, the mosquitoes are still being tested in cages, but even for that step the researchers spent years diligently consulting with local citizen groups, academics, regulators, and farmers. "We think that is the most ethical way to introduce a new technology like this," says James Lavery, a bioethicist at St. Michael's Hospital in Toronto, Canada, who works as a consultant for the project.

The World Health Organization (WHO) is still drafting guidelines for the release of transgenic mosquitoes, a process that will take at least three more months, says Yeya Touré, manager of innovative vector control interventions at WHO. Touré says he knew of the trial in Grand Cayman, and that he is not aware of any wrongdoing by Oxitec.

But environmental groups, taken by surprise, are lamenting what they see as a lack of openness. "If these mosquitoes are completely safe, then why the hush-hush?" says Gurmit Singh, chair of the Centre for Environment, Technology and Development in Malaysia, where Oxitec hopes to start a field trial soon as well. James-who also takes issue with Alphey's press conference to announce unpublished results—says it would be "unfortunate" if Oxitec's release in the Caribbean soured the climate for GM mosquitoes in general. Despite their differences, the collaborators are still on speaking terms, he stresses.

Not everybody thinks the release is such a big deal. Oxitec's transgenic mosquitoes are programmed not to have viable offspring, which makes it extremely unlikely unat any newly introduced genes would spread, says medical entomologist Willem Takken of Wageningen University in the Netherlands. The company's technology is just a modern version of the so-called sterile insect technique (SIT), he says, in which massive numbers of male insects are sterilized by bombarding them with radiation and then released. Half a century old, SIT has been used safely and with great success against a range of agricultural pests (Science, 20 July 2007, p. 312).

Stickier issues arise with different strategies that don't try to reduce natural populations to zero but replace them with new ones unable to transmit disease, says John Marshall of Imperial College London. To achieve that, researchers try to find genes that make insects resistant to infection and make these genes spread through the entire population. That approach, which so far has proved elusive, is fraught with ethical and regulatory problems because its explicit goal is to spread genes far and wide.

Ethics and communication strategy aside, researchers say the results of the trial, if they hold up under peer review, are encouraging. Oxitec's technique offers the promise of an environmentally friendly way to reduce mosquito populations and, thus, to control disease, says Marcelo Jacobs-Lorena of Johns Hopkins University in Baltimore, Maryland. It also has an edge over insecticides because it's hard to see how mosquito populations could develop resistance to suicide genes. He thinks the stealthy trial will have a positive impact on the field: "There's too much caution and too much fear of the unknown. This study may help surmount that."

-MARTIN ENSERINK

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Whoever figures out how to predict the stock market will get rich quick. Unfortunately, the market's ups and downs ultimately depend on the choices of a massive number of people—and you don't know what they're thinking about before they decide to buy or sell a stock. Then again, maybe Google knows. A team of scientists writing in Philosophical Transactions of the Royal Society A has shown a strong correlation between queries submitted to the Internet search giant and the weekly fluctuations in stock trading. http://scim.ag/Google-stocks

Physicists Create Black Hole 'Light' in Lab

Thirty-six years ago, Stephen Hawking, the famed British theoretical physicist, predicted that black holes—from which no light should escape—could, paradoxically, emit light. No one has ever observed this "Hawking radiation," but now, physicists report in Physical Review Letters that they've created something very much like it in the lab. http://scim.ag/hawking-light

Whales Get Sunburns, Too

In these ozone-depleted times, most of us reach for a T-shirt or a bottle of sunscreen to protect us from the sun's ultraviolet radiation. Whales don't have those luxuries—and they're paying the price. In Proceedings of the Royal Society B, researchers report numerous cases of sunburned and blistered skin on whales in the wild, sparking concern that the thinned ozone layer may be causing skin cancer in these animals. http://scim.ag/whales-burn



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