



Cayman demonstrates RIDL® potential

In November, the Cayman Islands Mosquito Research and Control Unit (MRCU) together with Oxitec announced the results of a trial carried out on Grand Cayman last summer. Around 3 million male sterile mosquitoes were released over several months. These releases reduced the local population of the dengue mosquito *Aedes aegypti* by 80%.

MRCU and Oxitec staff set up a local rearing unit where eggs, sent from Oxitec UK, were hatched and reared. Sterile male mosquitoes were then released at multiple locations throughout the release area. Egg counts and capturing of adults were carried out throughout the trial using standard ovitraps and adult traps called BG sentinels.

The world's first release of GM mosquitoes

All release points and trap data were integrated on a GIS mapping system. The target release rate of RIDL mosquitoes was achieved in July; the target population then started to decline sharply in August, reducing the population to minimal levels by October. Together with a preliminary experiment in late 2009, this was the world's first release of GM mosquitoes; the successful suppression of a wild population is a striking validation of Oxitec's technology. All trial objectives were met.

Male mosquitoes, unlike females, do not bite and so cannot spread disease; hence releasing only males provides no increased health risk. The females take blood meals from humans to provide nutrition for their eggs and in so doing spread diseases such as dengue, chikungunya and yellow fever. The males on the other hand feed on plant juices or sugary saps. In fact, the males do not even have the right mouthparts for biting.

The announcement of the trial result prompted much positive media coverage, some of which is captured on our [website](#) under 'our news'.



Preparing for releases in Cayman

Brazil evaluates RIDL® for Dengue

In December Brazil's National Biosecurity Technical Commission (CTNBio) approved the go ahead of open trials in 2011 to evaluate the potential for Oxitec's OX513A strain to control the dengue-carrying mosquito *Aedes aegypti*. This approval follows similar initiatives in the Cayman Islands and Malaysia.



Typical village street in the trial site region

The trials will take place in Brazil's northeast, supervised by Dr Margareth Capurro of the University of São Paulo, and will involve Brazil's leading sterile insect technique organisation,

Moscamed. This company developed the radiation-based sterile insect technique within Brazil to control agricultural pests but sees Oxitec's RIDL approach as an important alternative to control dengue. Moscamed and Oxitec have worked closely to establish the facilities and prepare staff.

Brazil is particularly affected by dengue. Since the mid 1970s dengue has grown at an alarming rate with a record number of cases reported in 2010. Dengue is a key priority for Brazil's Ministry of Health which has set up a national programme for dengue control.

Public engagement is key to the trials. Moscamed has already held a public workshop attended by key stakeholders such as national and local health officials, members of the public and the media. An ongoing programme of public consultation and engagement is being carried out in parallel with the trials.



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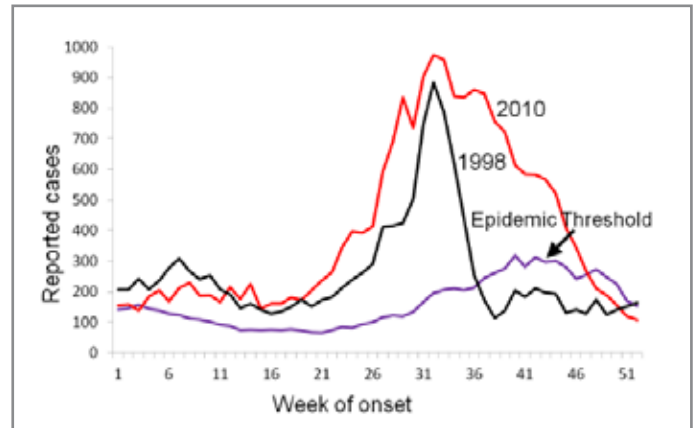


Dengue 2010 review

Globally, the number of cases of dengue fever continued to rise in 2010. In a number of countries reported cases and deaths have reached a record. This is the case in Brazil where the Pan American Health Organisation reported 1.2 million cases and 673 deaths. In the same region, Columbia, Honduras and Venezuela have all reported dengue cases at record levels. Other regions of the world saw the same pattern: that of more cases of dengue and its expansion into new countries.

In many regions, dengue has reached record levels

As there is neither medication nor vaccine, controlling dengue relies solely on controlling the mosquito that spreads the disease. While conventional control methods such as the use of insecticides can have an impact locally, for a limited period, gaining overall control of the problem remains a huge challenge. Once *Aedes aegypti* inhabits a new territory it is remarkable resilient to current control methods. Singapore, for example, is considered by many to have the most organised and intensive control campaigns aimed at reducing or eliminating dengue-carrying mosquitoes. However despite this, there were 5,364 reported cases in 2010, a 19.3% increase on 2009.



Reported dengue cases in Puerto Rico, 1998 and 2010
(Source: CDC Vol 3 No. 1 2011, February 16, 2011)

The Centre for Disease Control and Prevention reported in the February 2011 Dengue Update that dengue is having an increased impact on the US with historically high levels of cases in Puerto Rico (see graph, above), US Virgin Islands and Florida. Puerto Rico reported over 21,000 cases in 2010, the largest outbreak in its history. About 75% of these could be confirmed through laboratory tests with dengue 1 and dengue 4 being the predominant serotypes. As many cases are not reported the actual incidence rate was probably much higher.

With neither medication nor vaccine, controlling dengue relies solely on controlling the mosquito that spreads the disease

Aedes aegypti has been present in Florida for several years. In 2009 there were 27 cases of locally acquired dengue cases in the Keys. A serosurvey of residents suggested an infection rate of 5%, indicating a serious risk of transmission. Despite an intensive control programme in 2010 the number of cases then rose to 63 cases in Key West, one in Broward County, and one in Miami-Dade County. There had not been an outbreak in Florida since 1934.

Last year two local Dengue infections were reported in Nice, France. It is the first time that natural transmission of the dengue virus has been reported in continental Europe since 1927-1928 according to the European Centre for Disease Control and Prevention.

The overall increase in dengue in 2010 and the difficulty of controlling of the mosquito that spreads the virus both support the urgent need for new control measures.

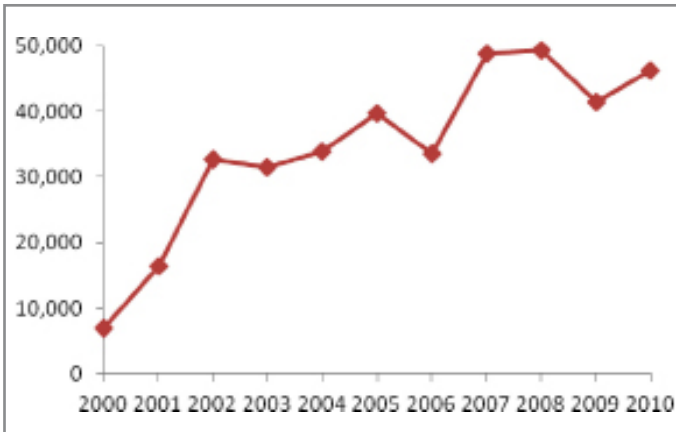


Aedes aegypti biting

It is probable, though not certain, that *Aedes aegypti* has reached – or is near to reaching – its geographic limits. However the virus has not. Once the virus is brought into a locality for the first time, the fact that the mosquito is already there means that the conditions already exist for rapid disease outbreak. This explains the concern of health officials in countries where locally acquired dengue is reported for the first time. Furthermore there are four different versions or 'serotypes' of the virus. Subsequent infections of a different serotype in an area can lead to worsening outbreaks, both in incidence and severity.



Malaysian field trial goes ahead



Malaysia: Reported cases of dengue (Source: WHO)

Oxitec's lead *Aedes aegypti* product, OX513A, has been released in the first ever outdoor trial of GM mosquitoes in Asia. This landmark trial is the first in an expected series of trials in Malaysia to demonstrate the potential of OX513A to control the mosquito that spreads dengue fever and chikungunya.

This first trial studied the longevity and dispersal of Oxitec's male sterile mosquitoes and compared them to wild ones. Some 6,000 OX513A males were released in an area near Bentong, Pahang State, with 6,000 wild males. The trial was carried out by Malaysia's Institute for Medical Research, a result of a long collaboration between Oxitec and Malaysia's Ministry of Health. The results will be published shortly.

Malaysia already has several 'firsts' in working with Oxitec to evaluate Oxitec's RIDL® technology for dengue: the first dengue endemic country to import this strain (2006), the first to conduct semi-field trials (2007-2008), dedicated workshops on risk assessment and risk communication, and extensive consultation with numerous committees, the public and NGOs (2009-2010).

Public engagement is vital for all such trials and media discussion has been ongoing. An independent survey conducted by a leading Malaysian newspaper showed that Bentong residents were happy with the government's plan to release GM mosquitoes to overcome dengue (*The Star*, 31 October 2010).

Malaysia, like many countries, has seen a sharp increase in dengue in the past decade. In 2010 the number of cases rose by 11% on 2009 and there were 134 deaths. Controlling the insect that transmits the virus between humans is critical, and the Malaysian government is evaluating Oxitec's technology as part of its Integrated Vector Management programme.



Local dengue health warning, asking people to check their homes for *Aedes* breeding sites

'Boldness' nomination

Oxitec has been nominated in The 2011 *Financial Times* ArcelorMittal Boldness in Business Awards Newcomer category, which was last year won by social media company Twitter. These annual awards highlight innovative and dynamic companies and entrepreneurs.

Boldness in Business is described as the willingness to venture where others fear to tread and to push the edge of the proverbial envelope, qualities that will make the vital difference in these challenging economic times. Nominations are made by *Financial Times* (FT) journalists with a shortlist created by the FT editing panel. PricewaterhouseCoopers act as technical consultants. Other categories cover Drivers of Change, Entrepreneurship, the Environment, Emerging Markets and Corporate Responsibility.

This year's nominees include companies like Apple, Facebook, Danone and Metrobank, so the competition is tough! For more information see: <http://www.ftconferences.com/boldness/>





First results from trials for RIDL® olive fly

As reported in the October newsletter, olive fly is the major pest of commercial olives throughout the Mediterranean and California. Traditional controls make heavy use of chemical insecticides (mainly organophosphates and pyrethroids). As older chemicals are withdrawn from market, the farmer's choice is more restricted. Frequent exposure to these chemicals increases the rate at which the olive fly develops resistance. Resistance is now being seen in even the most recently introduced chemicals such as Spinosad® and farmers are running out of control options. Alternative strategies – such as pheromone disruption, parasitoids, and lures and traps – tend to be costly and ineffective against high infestations.

Oxitec has developed a RIDL olive fly strain (OX3097D). Testing earlier last year at the University of Oxford showed very promising early results. In these second phase trials carried out in collaboration with the University of Crete's Department of Applied Entomology, we conducted

a series of mating and re-mating tests in a contained environment using wild olive flies collected from the heavily infested olive orchards surrounding Crete's capital, Heraklion. Such studies are critical in assessing the potential of our strain to control an olive fly population. We aim to see whether the RIDL males are able to compete with the wild males for the females.

Initial results are extremely encouraging. The OX3097D males obtained 44% of copulations from 10 separate mating competitiveness tests with over 300 couples analysed. Moreover, less than a quarter of the wild females attempted a re-mating within their lifetime, and of those females that did re-mate, no preference for wild or OX3097D males was observed. These initial results strongly suggest that the OX3097D males are highly competitive against their wild counterparts. Further testing will be carried out prior to open trials next year which are subject to regulatory approval.

