OXITEC'S FAILED GM MOSQUITO RELEASES WORLDWIDE:

Forewarnings for Africa and the Target Malaria project

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The African Centre for Biodiversity (ACB) has a long and respected track record of research and advocacy. Our current geographical focus is Southern and East Africa, with extensive continental and global networks. We do research and analysis, advocacy and skills sharing and seek to inform and amplify the voices of social movements fighting for food sovereignty in Africa.

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Acronyms and abbreviations

CPB	Cartagena Protocol on Biosafety
DHF	Dengue haemorrhagic fever
EPA	Environmental Protection Agency
EU	European Union
FDA	Food and Drug Administration
fsRIDL	Female sex-RIDL
GBIT	Gangabishan Bhikulal Investment and Trading Limited
GM	Genetically modified
LMOs	Living modified organisms
MRCU	Mosquito Research and Control Unit
RIDL	Release of insects carrying a dominant lethal genetic system
UKTI	United Kingdom Trade and Investment
USDA	United States Department of Agriculture
WHO	World Health Organisation

About this **briefing**

Genetically modified (GM) mosquitoes were first released into the environment a decade ago, in the Cayman Islands. However, the Cayman Islands government recently announced an end to these experiments, stating that they had been a failure. Experiments in Malaysia and Panama have also ceased and plans to release GM insects in many other countries have been quietly abandoned.

All the GM insects that have been released into the environment to date were released as part of experiments by the UK-based company Oxitec, which is now owned by the US biotech company Intrexon.

This briefing summarises what is known about the releases of GM insects that have been made worldwide to date, including impacts on human health and the environment and the role of regulations and public engagement in decision-making. It asks what the lessons are for Africa regarding Target Malaria's plans to release GM mosquitoes in Africa. [1,2]

1. The GM insect company **Oxitec**

Oxitec is a UK-based commercial company, which produces genetically modified (GM) mosquitoes and other insects.[3] In September 2015, Oxitec was acquired by the US-based synthetic biology company Intrexon.[4]

Oxitec was originally a spin-out company from the University of Oxford and the main early-stage investors were the University, Oxford Capital Partners and East Hill Management.[5] In September 2015, Intrexon acquired Oxitec for $160 million (paid in a mix of cash and stock).[6] Claims of evidence of success of their trials on GM mosquitoes featured heavily in press releases made by the two companies at the time, including claims of "*over 90% reduction of the* Aedes aegypti [mosquito] *population*".[7,8] The *Aedes aegypti* species of mosquito transmits the tropical diseases dengue fever, zika and chikungunya. However, the companies' claims are not supported by the evidence now available about these trials.[9]

2. Oxitec's GM **insects**

Oxitec's GM insects are living modified organisms (LMOs) that can fly and spread widely in the environment. For example, mosquitoes spread on people's clothes and in habitats such as car tyres, and insect pests spread around the world on plants, fruits, vegetables and animals, including via planes and ships. Unlike GM crops, which are intended to remain within the fields where they are planted, GM insects are intended to spread and mate with wild insects.

Oxitec's patented technique for genetically modifying insects is known as RIDL (release of insects carrying a dominant lethal genetic system).

The company's open field experiments to date mainly involve its OX513A strain of the *Aedes aegypti* mosquito, which is genetically engineered to contain a red fluorescent marker and the RIDL "conditional lethality" trait.[10] The mosquitoes are genetically engineered to die at the larval stage in the absence of the antibiotic tetracycline, which acts as a chemical switch to allow breeding in the laboratory. Although Oxitec frequently describes its GM mosquitoes as "sterile", this is not the case. Oxitec's male GM mosquitoes are intended to mate with wild females and produce male and female offspring carrying the genetic trait, most of which die at the late larval stage. Repeated releases of many millions or billions of GM males, vastly outnumbering the wild male mosquito population, are intended to reduce the total adult population of mosquitoes over time.

As well as GM mosquitoes, Oxitec is developing GM agricultural insect pests, such as fruit flies, diamondback moths, bollworms and olive flies. Oxitec's technique for GM agricultural pests is known as fsRIDL (female sex RIDL). These insects use a variation of the trait in which only the female offspring are genetically engineered to die.[11] Oxitec is seeking to apply the same approach to fall armyworm (a pest for more than 80 kinds of plant, including maize, rice, sugarcane and cotton).[12] If it is successful, GM fall armyworms might also be marketed in Africa. However, the company has yet to publish any evidence that it has genetically engineered this pest, let alone that this could be successful in the field.

Since 2018, Oxitec has also begun open release experiments in Brazil with a new version of its GM mosquito, which, like its GM agricultural pests, is female-killing only (i.e. only the females of the GM insects are killed by the genetic trait).[13]

Oxitec's business plan is dependent on locking its customers in to repeated payments for ongoing releases of its GM insect species, with the aim of keeping the target wild species' numbers low.

3. Open releases of **Oxitec's GM insects**

Since 2009, Oxitec has conducted experimental open releases of genetically modified (GM) mosquitoes in the Cayman Islands, Malaysia, Brazil and Panama. It has also conducted a small experimental release of GM diamondback moths (a pest of cabbages and other crops) in the USA. Only releases in Brazil continue at the present time, and these are now using a new version of Oxitec's GM mosquito, which has yet to be released elsewhere. The company claims this new technology will be more effective: however, the company has not published any evidence to support this new claim.

Oxitec has previously claimed that it will conduct open releases of GM mosquitoes in Colombia,[14] the USA,[15] India,[16] Pakistan,[17] Singapore,[18] Argentina,[19] Ecuador, Costa Rica,[20] Puerto Rico[21] and elsewhere in the Caribbean.[22] However, none of these projects have happened in reality. Caged trials of a different version of Oxitec's GM mosquitoes (flightless

females) took place in Mexico but were abandoned after the GM mosquito line was reportedly discovered to be contaminated.[23]

In 2018, the Environmental Health Minister in the Cayman Islands confirmed that trials of Oxitec's GM mosquitoes there did not work and would be abandoned.[24] Oxitec's releases of GM mosquitoes in Panama and Malaysia ceased earlier, due to concerns about costs, effectiveness and risks. In Malaysia, trials were abandoned following a small open release experiment to measure flying distances and survival rates.[25] The health ministry concluded that "*the method was not practical besides involving high costs*".[26] In Panama, open release trials of Oxitec's GM mosquitoes were conducted in 2012 and then ceased, reportedly due to the high costs.[27] Proposed trials in other countries never actually took place. For example, Gangabishan Bhikulal Investment and Trading Limited (GBIT) is an Indian commercial company that has been working in partnership with Oxitec since 2011.[28] However, no open releases of Oxitec's GM mosquitoes have taken place in India. Oxitec notes that its former subsidiaries in Singapore, Mexico, Australia and Costa Rica are all now dormant.[29] Since its Cayman Island operations have now closed,[30] only the company's Brazilian office remains active.

In Brazil, several trials of Oxitec's OX513A GM mosquito strain have taken place with the approval of the biotech regulator CTNBio. However, commercial releases have never been approved by the Brazilian health authority ANVISA, which wants to see evidence of benefits to health before giving its approval, in line with recommendations from the World Health Organisation (WHO).[31,32,33]

In Brazil, Oxitec released GM mosquitoes in Jacobina and Juazeiro in the state of Bahia, from 2011 to 2013. In 2016, Oxitec began larger-scale trials of its GM mosquitoes in Piracicaba, a city located in the state of São Paulo.[34] However, in 2018, Oxitec Brazil decided to close its GM mosquito factory in Piracicaba.[35] According to the company, the reason was the transition to a newer version of its GM mosquitoes, known as OX5034, which began to be released in a pilot project in Indaiatuba in the Campinas region, in mid-2018. In November 2018, Oxitec announced that in

future it would only conduct trials with this new generation of GM insects, which, like its earlier GM pests, are female-killing only (i.e. only the females of the GM insects are killed by the genetic trait).[36]

Further proposed trials of Oxitec's GM mosquitoes in the USA (in Key Haven, Florida Keys) were halted in 2016 following a local vote against the trials and the threat of legal action.[37] The Food and Drug Administration (FDA) authorisation for the Key Haven trials was withdrawn[38,39] and a new authorisation will be needed from the Environmental Protection Agency (EPA) if any future trials are to go ahead.[40] Now that it has switched to its newer female-killing OX5034 strain of GM mosquito, Oxitec will need to submit a new application to the regulators.[41]

Oxitec has sought to release GM diamondback moths in the UK[42,43,44,45,46,47,48,49] and the USA,[50] GM olive flies in Spain,[51,52] and GM fruit flies in Australia[53] and Brazil. All these GM agricultural pests are female-killing only. Only one of these open release experiments has taken place. This was a small-scale "mark-release-recapture" experiment, using GM diamondback moths, in New York State in 2017.[54] Despite an application to conduct population suppression experiments with these GM moths, a permit was not granted.

Earlier, open release experiments were conducted in Arizona in 2007 and 2008, using Oxitec's GM pink bollworms (a cotton pest), with only the fluorescence trait for identification purposes (not the RIDL "conditional lethality" trait), and made sterile using radiation.[55] Although they used irradiated sterile insects, with only a GM fluorescence trait, the GM bollworm experiments were halted, partly over US organic farmers' concerns about contamination of their crops with genetically modified organisms (GMOs).[56,57] They also led the United States Department of Agriculture (USDA) Office of Inspector General to make a highly critical report, which argued that the USDA's controls over GM insect research were inadequate and that regulations needed to be strengthened.[58]

4. Concerns about **efficacy and risks**

> "Whilst Oxitec and MRCU are making public statements proclaiming major reductions in the Aedes aegypti population in the treatment area the data I have seen does not support this."
>
> **Cayman Islands' Mosquito Research and Control Unit (MRCU) scientist, 4 April 2017[59]**

> "To date all the measures recorded have shown no significant reduction in the abundance of Aedes aegypti in the release area."
>
> **MRCU scientist, 4 April 2017[60]**

Oxitec has repeatedly claimed that its experiments have been successful. In a brochure published in 2016, the company stated, "*Oxitec has developed a paradigm shift in mosquito control leading to unparalleled levels in the suppression of* Aedes aegypti*, the main vector for several of the world's most damaging viruses including zika, dengue and chikungunya*" and, "*In five separate efficacy trials across three different countries, releases of Oxitec OX513A mosquitoes led to a greater than 90% reduction in the local* Aedes aegypti *populations*".[61] However, these claims are not supported by the evidence.[62] Oxitec's decision to stop releasing its OX513A mosquito and begin trials with a new female-killing version effectively confirms that its trials to date have all been a failure. There is no commercial approval for releases, as the company lacks any evidence of efficacy in tackling dengue or other diseases spread by this mosquito.

Further, GM mosquito production is extremely costly and there have been production problems. In 2014, the release of 300,000 GM mosquitoes in Panama was reported to have cost $620,000 (more than $2 per mosquito).[63] In the Cayman Islands, production issues included the release of a high percentage of female GM mosquitoes (discussed later in this briefing), high adult and larval mortality, and mould in the rearing unit. [64]

Hype about the claimed "solution" provided by Oxitec's GM mosquitoes can result in significant opportunity costs if investments are diverted from more effective existing tools or more promising research and development by unrealistic promises.

In addition, Oxitec's open releases of GM mosquitoes pose risks to local human populations and their environment. A few examples of these risks are discussed below.

4.1 Risks of GM mosquitoes with the RIDL "conditional lethality" trait

Until recently, all Oxitec's open releases of GM *Aedes aegypti* mosquitoes used their "conditional lethality" trait, which aims to kill both the male and female offspring of the GM mosquitoes before they reach adulthood (mostly at the larval stage). Some of the risks associated with these releases are discussed below.

4.1.1 Release of female GM mosquitoes

Although Oxitec has often stated that it would release only male GM mosquitoes, this is not the case. Oxitec produces GM male and female mosquitoes, then sorts them to try to remove the females prior to release. Some GM females are inadvertently released, due to difficulties with the process of sorting males and females. In addition, the genetic trait is passed on

to both the male and female offspring that are produced when the released GM male mosquitoes mate with wild females. Some of these GM female larvae will also survive to adulthood. GM female mosquitoes can bite humans and transmit disease. Because of the very large numbers released, even a small proportion of biting female GM mosquitoes may lead to a large number in the releases.

Emails released as a result of a Freedom of Information (FoI) request in the Cayman Islands highlight "*a significant increase in the number of female mosquitoes collected in the treatment area*", rather than a decrease, which is thought to be due to the accidental release of GM female mosquitoes.[65] The emails reveal a high level of concern about the inadvertent release of GM female mosquitoes, from the MRCU scientist with access to the data.[66] A 2017 report includes female adult mosquito numbers collected from traps in the published data.[67] The graph shows significant increases (spikes) in adult female mosquito numbers in the release area five to seven weeks after the releases begin, and again seven to eight weeks after the releases were stepped up.

4.1.2 Effects on other mosquito species

Releases of Oxitec's GM *Aedes aegypti* mosquitoes are intended to suppress the wild population of *Aedes aegypti*. Unlike removing breeding sites or using larvicides, this is a single-species approach, which does not reduce populations of non-target species. If population suppression of *Aedes aegypti* is successful (even temporarily), one important question is whether *Aedes albopictus* (Asian tiger) mosquitoes, which also transmit dengue and several other viruses (including chikungunya), will increase in numbers and perhaps establish in new areas as a result of competitive displacement of one species by another. *Aedes albopictus* has been responsible for epidemics of dengue and chikungunya elsewhere in the world,[68,69] and for the re-emergence of dengue in southern China,[70] and this species is likely to play an important role in the maintenance and transmission of the virus.[71,72]

In a draft risk assessment submitted to regulators in the USA in 2011, Oxitec states: "*It is not clear to what extent Ae. albopictus could or would expand its range into areas currently dominated by* Ae. aegypti *but it is reasonable to expect a degree of such expansion if no countervailing activities are undertaken*".[73] Oxitec also published a paper in 2010, which uses computer modelling to show how *Aedes aegypti* and *Aedes albopictus* may interact.[74] The authors acknowledge that this could have important consequences for the persistence of disease. In its 2015 application to the Cayman Islands, Oxitec states, "*Should* Aedes albopictus *begin to occupy the* Aedes aegypti *niche upon reduction in their numbers, a concurrent operation will begin to reduce the numbers of* Aedes albopictus".[75] However, no such operation has ever taken place, so there is no evidence that it would be effective or cost-effective; and in any case, Oxitec appears to have abandoned its work on GM *Aedes albopictus*, which is no longer mentioned on its website. More recently, Oxitec's former Chief Scientific Officer, Luke Alphey stated, "*Since* Aedes aegypti *and* Aedes albopictus *are known to compete ... it is possible that the successful implementation of ...[GM mosquito] gene drives could lead an existing* Ae. aegypti *population to be displaced by* Ae. albopictus *where it would not otherwise have been. This would likely hamper efforts to eliminate viruses such as dengue since* Ae. albopictus *are also competent vectors...*".[76]

4.1.3 Impacts on target mosquito population numbers and on dengue fever

Other possibilities are that mosquito numbers in areas neighbouring the trials could increase as a result of the experiments; a rebound in mosquito numbers or cases of disease could occur when releases cease; or partial population suppression could increase the risk of the more severe form of the disease, dengue haemorrhagic fever (DHF). These possibilities are risks to public health associated with undertaking trials in dengue endemic areas and are explained below.

The first issue to consider is whether releases of GM mosquitoes could cause an increase in the numbers of mosquitoes in surrounding areas. This effect is predicted by some models for the release of sterile insects.[77] There is evidence from Oxitec's experiments that numbers in neighbouring control areas may increase as the population is suppressed in the target area: however not enough evidence has been published to be certain of the cause.

There appears to be a real possibility that some of the wild mosquitoes, when swamped by very high releases of GM males, simply migrate to mate in the surrounding area, potentially increasing health risks for the people there.

A second issue is whether there could be a rebound in mosquito numbers and/or cases of disease. A model of Oxitec's releases in the Cayman Islands predicts a rebound in mosquito numbers when population suppression ceases.[78] Another possibility is that there is a rebound in number of dengue cases due to loss of human immunity.[79,80,81] If Oxitec were to be successful in temporarily suppressing the wild mosquito population, this is a possible mechanism through which the number of dengue cases could increase as a result of Oxitec's experiments, especially if a reduction in the mosquito population cannot be sustained.

Perhaps the most important issue is whether cases of the more serious dengue haemorrhagic fever (DHF) might increase as a result of the experiments. In its draft risk assessment submitted to regulators in the USA Oxitec states: "*It has been suggested that, in countries with very high transmission rates, reduction in transmission could increase the frequency of dengue hemorrhagic fever (DHF) even while decreasing the incidence of dengue fever*".[82] The mechanism is a possible loss of cross-immunity to multiple serotypes of dengue.[83,84]

This is an example of how unintended effects can arise from the complex interactions between mosquito numbers, human immunity and the incidence of a disease.

4.1.4 Survival and spread of GM mosquitoes and impacts of antibiotic resistance

Oxitec's GM mosquitoes are programmed to die at the late larval stage in the absence of the antibiotic tetracycline. However, there are several mechanisms which could allow many more of the mosquitoes to survive to adulthood.

In the laboratory, 3% of the offspring of Oxitec's GM mosquitoes survive to adulthood, even in the absence of the antibiotic tetracycline.[85] When GM mosquitoes were fed cat food containing industrially farmed chicken, which contains the antibiotic tetracycline, the survival rate increased to 15–18%. Oxitec originally hid this information[86] but later admitted to an 18% survival rate of larvae fed on cat food in a published paper.[87] Because tetracycline is widely used to treat humans and animals, it can be found in high concentrations in the environment, for example in septic tanks and animal manure. The presence of tetracycline in the environment means that at least some of Oxitec's GM mosquitoes, if they encounter the antibiotic, can survive to adulthood.

The use of tetracycline to breed the GM mosquitoes in the laboratory also carries the risk of spreading antibiotic resistance, which could pose a major risk to human and animal health. Insect guts are reservoirs for antibiotic resistance genes with potential for dissemination.[88,89] Insect production in factories exposed to antibiotics could lead to drug resistance in their microbiota so that the insects disseminate antibiotic resistance when released into the environment.[90,91]

The percentage of surviving GM mosquitoes could also increase if resistance to the genetic killing mechanism evolves over time.[92,93]

4.1.5 Introduction of new mosquito strains

To create its GM mosquitoes, Oxitec started with a strain of *Aedes aegypti* mosquito that is commonly kept in laboratories, which probably came originally from Cuba. Before releasing the GM mosquitoes into the environment, it crossed them with wild strains from Mexico (for the releases in the Americas) or Asia (for the releases in Malaysia). When Oxitec's GM mosquitoes breed with wild mosquitoes some of their other genetic characteristics will be passed on to the local wild mosquito population. Different wild strains of the same species are found in different places and some strains are more resistant to insecticides than others or better transmitters of disease.[94,95,96,97,98] The possible introduction of such traits needs to be considered. Harm to people's health can be increased if some serotypes or viruses can be transmitted more easily by the introduced strain than they were by the wild species already in the area, or if the strain is resistant to insecticides.

4.2 Additional risks of female-killing GM insects and agricultural pests

Oxitec's GM agricultural pests, such as fruit flies,[99] moths[100] and olive flies[101] raise additional concerns because they are female-killing only (they have what Oxitec calls its fsRIDL trait). The idea is that mass releases of GM males will mate with wild females and their offspring will contain the female-killing trait. This genetically engineered trait is intended to make most of the female offspring of these matings die before adulthood; however the male offspring are intended to survive and breed for multiple generations. In addition, wild female pests that have mated with the released GM males will lay eggs that inherit the GM female-killing trait inside the crop they feed on (such as olives, fruit or cabbages). GM larvae (maggots) that develop from these eggs will begin eating the crop before the majority of the female larvae die inside the crop. The male GM larvae that grow inside the fruit are expected to emerge and develop into adults as normal and to go on to mate with other wild pests, again passing on the female-killing trait. As a result, there is likely to be significant crop damage during the releases,[102] as the offspring of the GM pests feed on the crop for multiple generations, and, in addition, many dead GM larvae will contaminate the crop.

There is little published information about Oxitec's new female-killing strain of GM mosquito. However, concerns about the spread of the GM trait and other traits of the introduced strain will increase if GM males survive and breed for multiple generations. Depending on the details of the technology used, other new concerns may be identified. In caged experiments in Mexico using an earlier female-killing version (Oxitec's flightless female GM mosquitoes), the GM mosquito line was reportedly contaminated, so that half the GM females could fly and mate, rather than being unable to survive and reproduce.[103]

5. Regulatory and governance **issues**

Prior to releasing GM insects into the environment, Oxitec infiltrated decision-making processes around the world, with a view to influencing regulations, guidelines and decision-making about the release of genetically modified insects.[104] Subsequently, the European Ombudsman found that one of the experts involved in developing guidance for the risk assessment of GM insects in the EU had failed to disclose his conflicts of interest as an employee of Oxford University receiving joint grants with Oxitec to seek to influence GM insect regulation.[105] Oxford University made £9.2m when Oxitec was sold to the US company Intrexon.[106]

Reeves et al. (2012) note that there were "significant omissions" in the information made publically available prior to open releases of GM mosquitoes in the Cayman Islands and Malaysia and that this made it impossible to establish whether relevant hazards had been properly assessed.[107] They also highlight that the Cayman Islands had no enacted legislation relating to living GM organisms at the time of the first open release of GM mosquitoes there.

In Brazil, the regulator CTNBio did not wait for a new regulation on GM insects to be completed before approving releases of Oxitec's GM mosquitoes in 2010.[108] The approval followed a 2007 meeting in London, organised by United Kingdom Trade and Investment (UKTI), where it was agreed that Oxitec and the Ministry of Health's scientific institute Fiocruz should initiate a collaboration to evaluate Oxitec's technology in the field in Brazil, with a view to commercialising it, and that "*Brazil's current GM regulations are unlikely to hamper or slow down this step*".[109]

Oxitec's GM mosquitoes have been exported from European Union (EU) countries for open release into the environment elsewhere. Under EU law, the exporter should provide prior notification, including a publicly available environmental risk assessment that meets European standards, before exporting GM insect eggs for open release to foreign countries. This legal requirement arises because GM insect eggs are live genetically modified organisms (living modified organisms or LMOs) covered by the Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity. This Regulation (EC) 1946/2003 is important because it requires the exporter to provide a comprehensive, publicly available risk assessment that meets EU standards for GMOs intended for release into the environment. [110] The precautionary principle must be taken into account when applying this regulation.

Oxitec has a poor track record of meeting the transboundary notification requirements when exporting its GM mosquito eggs to other countries, but it has never been sanctioned for its regulatory failures by the United Kingdom government.[111,112,113] Instead, the UK government has promoted the technology heavily via UKTI as part of an economic strategy designed to boost exports of patented biotechnologies overseas[114] and has changed tax rules for venture capital to help fund the company.[115]

Further, it remains questionable whether Oxitec would be liable for any harm to the environment or human health, should problems occur. Oxitec has always used in-country partners to make the applications to regulators. Depending on whether the developer or the in-country partner is defined as the operator in national law, this could mean that the in-country partner is held liable if anything goes wrong, allowing the developer (based in a rich country) to walk away and not take responsibility or bear the costs for any future harm.

6. Social and ethical **issues**

Social and ethical issues can only be addressed by broadening out the public engagement process and by taking a precautionary approach. Oxitec failed to acknowledge the extent of the ignorance and uncertainty surrounding the complexity of ecosystem responses to its releases of GM insects and instead made unsubstantiated and unrealistic claims about what its GM mosquitoes could deliver. Hype about Oxitec's claimed "solution" to dengue led to opportunity costs, as alternative solutions were neglected, and closed down public debate about the best ways to tackle problems.

Researchers have described how the multiple programmes of "community engagement" undertaken during the open field releases of Oxitec's GM mosquitoes in Brazil served

primarily to publicise the releases, rather than to examine whether this was a politically accountable or publicly acceptable decision.[116] For example, in Brazil, Oxitec's public engagement included a jingle claiming that Oxitec's GM mosquitoes are "the solution" to dengue,[117] "*Let him into your house, He's the solution, He fights dengue and won't bite anyone, Protect your health, He's the good mosquito*". This did not allow for any debate about the efficacy of this approach, and implied that it was known to work, rather than that it was an experiment with potential risks. In addition, debate focused solely on the GM mosquito, and this diverted attention from alternatives, including broader issues such as improving social conditions, health care or medical interventions.[118,119]

There are significant opportunity costs when operational and research and development budgets are spent on Oxitec's technology. For example, the Cayman Island emails highlight that the MRCU scientist with access to Oxitec's data was disappointed that MRCU signed a $400,000 extension of the project as "*an as yet unproven technique*" and that in his view this could have funded 13 staff for one year "*which would have allowed us to treat all problem yards across the island on a once-weekly basis*"[120].

7. Future releases of **GM insects?**

One of the organisations that previously funded Oxitec's GM mosquitoes is the Bill & Melinda Gates Foundation.[121] The Gates Foundation now provides core funding to another GM mosquito project run by the research consortium Target Malaria.[122] This time the focus is on using GM mosquitoes to tackle malaria, rather than dengue, and therefore different mosquito species are being genetically modified, in different ways, although the aim is still to suppress wild mosquito populations.

The ultimate aim of Target Malaria is to use a "gene drive" system, which aims to ensure the genetically engineered trait spreads through the mosquito population in a self-sustaining way. However, the release of gene drive GM mosquitoes is at least five to ten years away. Instead, Target Malaria plans to first release a different GM mosquito in Burkina Faso in 2019. These are not gene drive mosquitoes, which are still being researched in the laboratory, but a different "male sterile" GM mosquito, where the genetic engineering causes the GM male mosquitoes to be sexually sterile.[123] The proposal to release up to 10,000 GM mosquitoes over the coming year is a training exercise for the researchers. Target Malaria has stated, "*While this first strain is unlikely to be useful in itself for malaria control, it will be an important tool in determining how modified mosquitoes behave in an African genetic context, and for enhancing research and regulatory experience in our partner*

countries".[124] Such a move to release potentially risky GM mosquitoes with no benefit for malaria control is unethical. However, it remains unclear when the proposed open release of 10,000 GM mosquitoes will take place, as there appear to be ongoing problems with breeding large enough numbers of GM mosquitoes in the laboratory (the first open releases were originally planned for 2018).

The planned release of 10,000 male sterile GM mosquitoes is expected to be followed by larger releases of other GM mosquitoes in future years. One possibility that Target Malaria is considering next is releasing (non-gene drive) GM mosquitoes, which are genetically engineered to bias the sex ratio of the next generation towards male mosquitoes (which do not bite or transmit malaria), with the aim of reducing the total number of mosquitoes that could reproduce.[125]

Although the GM mosquitoes that Target Malaria is aiming to release will be different from Oxitec's, many of the same concerns arise and have yet to be addressed. For example, there is a lack of fully informed consent to the planned experiments; poor compliance with regulatory requirements and a lack of public consultation; unjustified hype about what the experiments can deliver; a lack of transparency and public consultation; and a lack of debate about alternatives.[126]

Should releases of GM mosquitoes using a gene drive be proposed in future, this would raise significant additional concerns.

8. Conclusions

Open releases of GM insects – particularly GM mosquitoes – into the environment to date have not delivered on their promises. Misleading hype has led to significant opportunity costs and the exposure of people to unnecessary risks. These mistakes must be avoided in the future but run the real risk of being repeated in Africa, where there is growing distrust in African institutions' inability to create conditions of openness, transparency, inclusion, accountability and good governance and where biosafety capacity is either non-existent or sorely lacking.

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