Memorandum

Malaysia's GM Aedes mosquito planned release: ethical, legal and human rights concerns

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Introduction

In October 2010, Malaysia's National Biosafety Board (NBB) approved the release of male genetically engineered, also called genetically modified (GM) Aedes mosquitoes into the wild. This field release will make Malaysia one of the the first countries in the world to release GM *Aedes aegypti* mosquitoes OX513A (My1).[1] The only other country which has released GM Aedes mosquitoes is the Cayman Islands - a British overseas territory - in 2009 which has been controversial and questioned by the British and European Parliaments. Please note that the GM mosquitoes released on insular Cayman Islands are supposedly of a different variant i.e. OX513A.

The Malaysian GM Aedes mosquitoes known as OX513A (My1) were purportedly developed by the Institute for Medical Research (IMR), and the UK-based biotech company Oxitec based on OX513A.

According to the NBB which was only established in late May 2010, some 2000-3000 male GM Aedes mosquitoes OX513A (My1) will be released per day for two consecutive days or a single release of a total of 4000-6000 along with wild type male Aedes mosquitoes. These experiments may be repeated. This means that thousands of GM mosquitoes along with the wild type mosquitoes could be released into the environment, especially if these trials are repeated.

The mosquitoes will be released in uninhabited and inhabited sites in the districts of Bentong in Pahang and Alor Gajah, Melaka.

[1] See http://www.biosafety.nre.gov.my/app_field/nbb_decision.shtml

Despite the range of environmental and public health and safety issues and objections raised by scientists, Malaysian environmental groups and international organisations, it is highly worrying that the NBB, Ministry of Natural Resources and Environment (MNRE) has given the approval to IMR to go ahead with the GM OX513A (My1) release. Nationally, several groups including the Consumers' Association of Penang (CAP) and Sahabat Alam Malaysia (Friends of the Earth Malaysia) submitted concerns about the release of GM mosquitoes and raised valid questions to the Biosafety Department, MNRE and the Ministry of Health (MOH). However, it is unknown if the issues raised have been adequately addressed as no specific, official response was given. MNRE has only placed on its website a summary of issues from the public submissions, with some general responses that still do not go far enough to allay the fears and concerns.

In November 2010, international reports have revealed that Oxitec announced its GM Aedes mosquitoes field trials in the Cayman Islands only a year after the event. Oxitec announcement on 11 November of its GM mosquitoes field trials in the Cayman Islands has taken aback both the international scientific community and GM critics, as well as the local people of the Cayman Islands.[2]

In November 2010, the British Parliament deemed fit to question Oxitec's release of GM mosquitoes in the Cayman Islands. The questions include, among others: whether Oxitec engaged in proper consultation and notification with the British authorities; whether an EIA on the experiment was provided by Oxitec to the UK government; whether the local population was consulted and whether relevant documentation is available for public scrutiny; and whether government officials including Ministers had held meetings with Oxitec prior to the experimental release of GM mosquitoes and if so, whether the dates of these meetings and topics discussed will be made available. Similar questions have also been raised in the European Parliament (Appendix 1).

[2] GM Mosquito Trial Strains Ties in Gates-Funded Project
http://news.sciencemag.org/scienceinsider/2010/11/gm-mosquito-trial-strains-ties.html

Oxitec's earlier activities in India are also looked upon by the international scientific community as suspicious. In July 2009, news that Oxitec was planning to do GM mosquito trials in India took the Indian scientific community and government officials by surprise. Two years previously, the Indian authorities had rejected Oxitec's proposal to do the trials. But it entered 'through the back door' by tying up with a private company which has no previous experience in mosquito research. This has raised concerns among Indian scientists that experiments with alien strains of GM mosquitoes are now done in a private lab in the absence of strict government biosafety guidelines for GM insects.[3]

The lack of openness in Oxitec GM mosquitoes release in the Cayman Islands is repeated in Oxitec's collaboration with the Malaysian Institute for Medical Research (IMR). The lack of transparency, the absence of meaningful and effective public participation, and the seeming haste in the approval process to release the GM mosquitoes for field experiments in the Malaysian case is setting a dangerous precedent.

Given this background, there are serious ethical, legal, public health and human rights issues involved which have not been sufficiently addressed by the Malaysian authorities. Hence, our new concerns include the following:

1. Non-transparency of GM Aedes trials and releases in the Cayman Islands:

Oxitec and its collaborators have not been transparent with the GM mosquito trials and release. According to a recent damning report on the SciDevNet[4] on 11 Nov. 2010, the release of GM mosquitoes in Cayman Islands was not announced internationally by Oxitec until after one year of the release, thus eliciting serious concerns among international biosafety experts.

The GM mosquitoes released on Cayman Islands had not been mentioned at the fifth meeting of the Parties to the Cartagena Protocol on Biosafety in October 2010 - which

[3] http://www.gmwatch.org/
[4] http://www.scidev.net/En/news/gm-mosquito-wild-release-takes-campaigners-by-surprise.html

addresses international safety issues relating to GM organisms — in Nagoya, Japan. Dr Luke Alphey, Chief Scientific Officer of Oxitec reportedly said that he did not know what the Nagoya meeting was.

This, despite Dr. L. Alphey being involved in the much touted **MosGuide**.[5] It is indeed strange for Oxitec not to know about and not to inform the Biosafety meeting in Nagoya or even prior to that, given that Oxitec has a Regulatory Affairs Manager, Ms. Camilla Beech, who was mentioned in the Oxitec staff website[6] as a member of both US (BIO) and European Inter-industry groups (EUROPABIO) on The Cartagena Biosafety Protocol, Convention on Biological Diversity. Further, Oxitec's non-executive team members include Dr. D. Brookes (chairman) and Dr. D. Buckeridge who advise the UK government on Technology Foresight for Environment and the UK Ministers on policy related to biotechnology and genetically modified organisms, respectively.

Hence, Oxitec should have been familiar with the Cartagena Biosafety Protocol and its biosafety registries[7] i.e. (i) The **LMO-Unique Identifiers Registry (LMO-UIds)**, which provides summary information on all living modified organisms registered in the BCH including transformation events, genetic modifications, and the unique identification code (if available) for each record. Links to all decisions that refer to these organisms are provided at the bottom of each LMO record accessible through the registry; (ii) The **Gene Registry**, which provides summary information on gene inserts and characteristics of the genetic modifications of LMOs; and (iii) The **Organism Registry**, which provides summary information on parental, recipient or donor organisms related to the LMOs registered in the BCH.

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[5] see his co-authored paper on Mosguide: Mumford J, Quinlan MM, Beech C, Alphey L, Bayard V, Capurro ML, Kittayapong P, Knight JD, Marelli MT, Ombongi K, Ramsey J, Reuben R (2009). *MosqGuide: A project to develop best practice guidance for the deployment of innovative genetic vector control strategies for malaria and dengue*. Asia Pacific Journal of Molecular Biology and Biotechnology 17(3) in press. (Source: http://www.oxitec.com/our-research/safety-and-regulation/ and http://www.mosqguide.org.uk/).

[6] http://www.oxitec.com/our-business/our-team/

[7] https://bch.cbd.int/database/organisms/

This gross oversight on the part of Oxitec was further compounded by a lack of public information and discussion. After the delayed international revelation of the release of Oxitec's GM mosquitoes on Cayman Islands, local islanders protested that they have not been informed beforehand i.e. no prior informed consent was sought. Oxitec has also been accused of using the Cayman Islands' as "a private lab", without public consultation or ethical oversight, and hence of colonial behaviour[8].

The way Oxitec went and is still going about with its GM mosquito releases is against the grain of ethical scientific research and genuine public participation, such that recently the House of Commons and the House of Lords seriously questioned the GM mosquitoes releases in the British Parliament.

Was the delayed announcement by Oxitec of the GM mosquitoes field trials in the Cayman Islands deliberate? Was the choice of Cayman Islands deliberate?

It seems that the Cayman Islands is a non-party to the Cartagena Biosafety Protocol and thus, the Protocol provisions do not apply. The UK's instrument of ratification of the Cartagena Protocol on Biosafety has not been extended to the Cayman Islands, an Overseas territory of the UK.

However, according to the UK Parliamentary Under-Secretary of State, Department for Environment, Food and Rural Affairs (Lord Henley),

"the shipment of the GM mosquito eggs from the UK was subject to the requirements of Regulation (EC) 1946/2003, chapter II of which imposes an obligation on exporters to notify their first intended transboundary movement of a GM organism to the relevant authority in the importing country, whether that country is a party or a non-party to the protocol, and to await its consent to proceed."[9]

[8] British Overseas Territory used as private lab for GM mosquito company, GeneWatch UK press release, 14 December 2010. http://www.genewatch.org/article.shtml?als[cid]=566989&als[itemid]=567324

[9] http://www.publications.parliament.uk/pa/ld201011/ldhansrd/text/101130w0001.htm#10113060000013

As such, it is very convenient for Oxitec to export the GM mosquito eggs to, and run the release experiments in the territories of a non-Party of the Cartagena Biosafety Protocol which has no or merely a weak experience in regulating living modified organisms. In the case of Cayman Islands, a local Cayman Island Department of Agriculture reportedly issued a permit, and a risk analysis and an environmental impact assessment were supposedly carried out, but have not been made public for analyses. There were no town hall meetings or public debates, leaving the public in the dark. While the Mosquito Research and Control Unit (MRCU) of the Cayman Islands did post on YouTube a video on the project, the clip fails to mention that the mosquitoes are genetically modified (GM).[10]

In comparison, if the field release is carried out in the UK, under British law, it has to be approved by the more stringent UK Department for Environment, Food and Rural Affairs (DEFRA) and would have to follow various EC rules and binding provisions of the Cartagena Biosafety Protocol.

Thus, the choice of releasing the GM mosquitoes in the Cayman Islands is similar to multinational corporations (MNCs) *modus operandi* (or operating methods) where they avoid the stringent environmental rules in developed countries by exporting their dangerous activities to developing countries, which have much weaker environmental rules and compliance mechanisms.

In view of the above, the officially stated Oxitec's business principles of being honest, open, trustworthy and adhering to all international and national laws and regulations are now in serious doubt.

2. Non-transparency of GM Aedes trials and planned releases in Malaysia:

In the case of Malaysia, being a party to Cartagena Biosafety Protocol, the provisions of the protocol are applicable. As such, the provisions of the protocol regarding the transboundary

[10] http://news.sciencemag.org/scienceinsider/2010/11/gm-mosquito-trial-strains-ties.html

movement of genetically modified (GM) organisms are applicable to the importation or shipment of Oxitec's GM mosquito eggs, juvenile or adults OX513A from the UK to Malaysia.

These original OX513A from the UK is what the IMR scientists have been working on in order to produce the subsequent OX513A (My1).

Malaysia, having been active in the Cartagena Biosafety Protocol, would have known the provisions of the Protocol that regulate the transboundary movement, transit, handling and use of all GM organisms '*that may have adverse effects on the conservation and sustainable use of biological diversity, taking into account risks to human health'*. Under its notification rules (Article 8), the exporter is required to inform in writing the competent authority of the Party of import prior to the intentional transboundary movement of a living modified organism for intentional introduction into the environment of the importing country.[11]

Similarly, Oxitec shipment of the GM mosquito eggs from the UK was also subject to the requirements of Regulation (EC) 1946/2003, chapter II of which imposes an obligation on exporters (i.e. Oxitec) to notify their first intended transboundary movement of a GM organism to the relevant authority in the importing country (i.e. MNRE, which is the national contact point for the Cartagena Biosafety Protocol) and to await its consent to proceed.

To our knowledge, there has been no publicly available evidence or report that the MNRE had given consent for the shipment of the GM mosquito eggs from Oxitec in the UK to IMR in Malaysia.

Further, there is no known proper risk analysis having been done. If there was a proper Risk Assessment (RA), it should be made public.

[11] http://bch.cbd.int/protocol/

And where are the Environmental and Social Impact Assessments (EIA and SIA)?

Please refer to more detailed discussion later in this memorandum.

3. Conflict of interests in Oxitec and close links with agrochemical MNCs:

It has been reported that Oxitec has been facing financial losses to the tune of some £1.7 million a year. It owes £2.25 million to a US investor which it is due to repay by 2013. It is clear that Oxitec is under tremendous pressure to commercialise its GM mosquito project to generate revenue.[12]

It must be noted that international publications such as the Proc Act Nat Sci USA (PNAS) has published a 'correction' on a conflict of interest statement omission related to Oxitec. Specifically, a paper co-authored by Dr. Luke Alphey of Oxitec previously published was corrected recently in Oct 2010:

"***APPLIED BIOLOGICAL SCIENCES*** *Correction for "Female-specific flightless phenotype for mosquito control," by Guoliang Fu, Rosemary S. Lees, Derric Nimmo, Diane Aw, Li Jin, Pam Gray, Thomas U. Berendonk, Helen White-Cooper, Sarah Scaife, Hoang Kim Phuc, Osvaldo Marinotti, Nijole Jasinskiene, Anthony A. James, and Luke Alphey, which appeared in issue 10, March 9, 2010, of* Proc Natl Acad Sci USA *(107:4550–4554; first published February 22, 2010; 10.1073/pnas.1000251107).*

The authors note that their conflict of interest statement was omitted during publication. The authors declare that those authors affiliated with Oxitec Limited (as noted in the author list) are or were employees or collaborative students of this company, which therefore provided salary and other support for the research program. Also, such employees may have shares or share options in Oxitec Limited. Both Oxitec Limited and

[12] Oxitec's genetically-modified mosquitoes: in the public interest? GeneWatch UK briefing. December 2010. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Oxitecbrief_fin.pdf

Oxford University have one or more patents or patent applications related to the subject of this paper."[13]

Another example of a conflict of interest in publications related to Oxitec GM mosquitoes is a paper co-authored by Oxitec staff that the MNRE Biosafety unit had repeatedly and singularly cited as reference that there was no evidence of interspecific crossmating of GM *Ae aegypti* with *Ae albopictus*. The reference was a paper co-authored by Dr. Seshadri Vasan, a member of Oxitec UK and CEO of Oxitec Sdn Bhd (Malaysia).[14] He was not indicated in this 2009 paper as being from Oxitec. This paper also does not carry a conflict of interest statement, as is usually required in other reputable publications.

More conflicts of interest are posed by Oxitec's staff as being closely linked with big MNCs. According to Oxitec's own website, most of its staff formerly worked for many years with agrochemical and pharma giants such as Syngenta, Astra Zeneca, Bayer, Advanta, and MNL. For example, to quote from the Oxitec website[15]:

Hadyn Parry, Chief Executive Officer worked for 15 years at Zeneca/Syngenta and held various positions, including General Manager of Zeneca Plant Sciences and European Director and Global Head of R&D for Advanta, one of the world's largest seed companies. More recently he was CEO of MNL Pharmaceuticals.

Dr Vasan, Chief Executive Officer of Oxitec Sdn Bhd (Malaysia) previously worked in the USA as a consultant in the pharmaceutical and medical products practice of McKinsey & Company.

Camilla Beech, Regulatory Affairs Manager has extensive international experience in the regulation of biotechnology products and crops. She obtained commercial food approval in

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[13] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2972981/

[14] Lee HL, Aramu M, Nazni WA, Selvi S, Vasan S (2009). *No evidence for successful interspecific cross-mating of transgenic Aedes aegypti (L.) and wild type Aedes albopictus Skuse*. Tropical Biomedicine **26**(3): 312-319 (http://www.ncbi.nlm.nih.gov/pubmed/20237445).

[15] http://www.oxitec.com/our-business/our-team/

the UK for the first GM crop in Europe, and obtained registrations for numerous biotechnology crops in Africa, Asia and the Americas. She advised the Humanitarian Board for Golden Rice on regulatory matters (1997 to 2004), and was a member of both US (BIO) and European Inter-industry groups (EUROPABIO) on The Cartagena Biosafety Protocol, Convention on Biological Diversity and Plant made Pharmaceuticals. Her most recent post was International Regulatory Manager for Syngenta Biotechnology Inc., based in San Diego, California.

Oxitec's Chairman, Dr David Brooks, has twenty-five years' experience with ICI in the agrochemical market. His last position was as Vice President of R&D for ICI Americas where he was responsible for functions from discovery through product safety, registration and pilot plant manufacture to market development and technical service. He was a member of the UK Government Science and Technology Foresight Panel for agriculture and the environment.

Dr David Buckeridge has more than 20 years' management experience in the pharmaceutical, genomics and chemical industries, with a particular emphasis on agribusiness. He spent some eight years in Zeneca's agrochemicals and five years in Iowa, running the commercial operations for AstraZeneca's seeds business in the US. He became CEO of Advanta, then the largest independent agronomic seeds businesses in the world; this was acquired by Paine & Partners in 2004. Buckeridge served as a commissioner to the UK Government's Department of Trade and Industry Biotechnology Commission, advising Ministers on policy related to biotechnology and genetically modified organisms.

In view of the fact that Malaysia has worked hard for more than a decade towards ensuring biosafety issues are addressed in the Cartagena Biosafety Protocol, it appears to be ineffective when locally, GM mosquitoes are being released in a hasty manner 'in cooperation with' agribusiness and pharma companies and links.

In the case of Oxitec, it is selling us GM Aedes mosquitoes which it claims will help wipe out dengue fever. This technology is unpredictable and can be devastating. Oxitec's claim to success was based on preliminary results which they themselves had presented at a conference in November 2010. In fact the claims to success were declared just days after the experiment ended. What are Oxitec's criteria for success? Many in the scientific community are questioning Oxitec's claims, in the absence of a full long term environmental assessment as the unintended environmental impacts remain unknown.[16]

While Cayman Islands is small and insular (island), Malaysia is large and not insular. Oxitec's technology means that to effectively reduce the population of *Aedes aegyptii* mosquitoes in Malaysia, it will require the continuous release in great numbers of the GM mosquitoes into the environment. Even if one were to assume that the GM mosquitoes do reduce the population of *Aedes aegypti* mosquitoes at the release sites, there will be movement of *A. aegypti* from the surrounding areas into the release sites. How effective will Malaysia be, a bigger land mass with porous borders surrounded by much larger countries and teeming populations? According to Dr Lim Thuang Seng, an immunologist, the Cayman Islands will continue to face the threat of dengue, and there is evidence *Aedes albopictus* is becoming established in some cities where *Aedes aegypti* was eliminated.[17] The Cayman Islands (land area 200 sq km surrounded by sea) may succeed in eliminating *Aedes aegypti* but fail to prevent the reintroduction of the mosquitoes from external sources.

Moreover, the *Aedes albopictus* mosquitoes (native to Malaysia which also transmits dengue) is still around and will still continue to transmit the dengue fever. Does this mean another group of GM mosquitoes, this time *Ae. albopictus*, has to be developed and continuously released too? Oxitec is already developing GM *Ae. albopictus* mosquitoes, presumably in anticipation of this problem[18].

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[16] GM mosquito wild release takes campaigners by surprise http://www.scidev.net/en/news/gm-mosquito-wild-release-takes-campaigners-by-surprise.html

[17] GM mosquitoes will fail, and incur heavy costs Dr Lim Thuang Seng Nov 19, 2010 Malaysiakini http://www.malaysiakini.com/letters/148604.

[18] http://www.oxitec.com/our-products/asian-tiger-mosquito-control/

Malaysia will have to spend enormous amounts of money just to keep releasing more of the GM Aedes mosquitoes.

It is appropriate to ask how much of taxpayers' money is involved in this doomed experiment?

How much money is paid to Oxitec for its proprietary GM mosquito eggs and its services?

Why then is the government gambling on this high risk technology and its false solutions? Why are we compromising the national interests and the interests of our citizens by IMR going into such business ventures?

The touted claims of success are dubious if the Oxitec GM mosquitoes cannot accomplish what it is supposed to do. In the Terms and Conditions for the field release of GM mosquitoes set by the NBB/MNRE, it is stipulated that '*at the end of the field trial, fogging in a 400m radius is required. A second fogging should be conducted one week after the end-of-field-trial fogging*'.[19] This is rather ironic as the GM mosquitoes project was initiated because of the ineffectiveness of fogging to control the dengue epidemics in the country. In fact, the Aedes mosquitoes have acquired immunity to many of the fogging chemicals used. It would appear that under the NBB Terms and Conditions, fogging is now considered effective in eliminating the GM mosquitoes! Hence, public doubts increase on the effectiveness of Oxitec's GM Aedes mosquitoes and derivatives, as well as the NBB Terms and Conditions.

GM technologies can unleash unintended ecological and health consequences. GM technologies and the companies that push them do not reflect the needs of the people and communities. It is about maximising profits for the companies, control over monopoly

[19] http://www.biosafety.nre.gov.my/appfield/nbbdecision.shtml

patents, control over decision making and consolidation of power. Business interests, bureaucrats and experts are at the centre of control, not the public interests.

We need to be wary of the web of relationships among big corporations, scientists and governments. Often these links with corporations engenders a lack of transparency about their true operations. Individuals move among these organisations in a well coordinated and reinforcing process. Many individuals from biotech companies, consultancies, agribusiness and big Pharma are appointed to public positions where they set policies favourable to the big agri, pharma and biotech firms and later, they go back to their lucrative corporate jobs to reap the profits. When we open doors for these powerful corporations and their allies to push unproven biotech methods in crucial areas such as public health, long-term public interests lose out.

It behoves the government to be cautious of such unproven technologies and unethical companies.

4. The hidden 3 to 4% offspring of male GM mosquitoes and normal females actually survive into adulthood

The fact that this project involves the creation and propagation of a deadly insect and its eventual release in the natural environment means that it is a dangerous and risky enterprise. The outcome of this experiment is unpredictable: there are too many unknowns and it has never been done anywhere in the world, except on insular Cayman Islands using purportedly a different variant. Once these mosquitoes are released in the environment, there is no way one can capture or recall them. What happens when some of these GM mosquitoes survive and multiply and do not all die as planned? What guarantee is there that these survivors will not mutate and become ‘frankenstein mosquitoes’ carrying new lethal diseases?

Scientific reports have demonstrated this possibility, for instance please refer to the extract of Prof. Cummins and Dr. Mae-Wan Ho's (of I-SIS) 2008 submissions to the US FDA and EPA on GM mosquitoes in the box below.[20]:

" The most glaring aspect of the proposed release is that the lethally acting transcription activator tTAV has a rather ill-defined action. The information presently available does not tell us what is killing the target animals. Even though a homologous tetracycline-repressed gene was not toxic to mice upon its activation, the killing toxin in the mosquito should certainly be identified before released to the environment is contemplated.

Another major hazard is horizontal gene transfer of the *piggyBac* insert. This issue has been thoroughly addressed in ISIS' submissions to the USDA with regard to the release of the pink bollworm in 2001. We provided evidence that the disabled vector carrying the transgene, even when stripped down to the bare minimum of the border repeats, was nevertheless able to replicate and spread, basically because the transposase function enabling the *piggyBac* inserts to move can be supplied by 'helper' transposons. Such helper transposons are potentially present in *all* genomes, including that of the mosquito. The main reason for using transposons as vectors in insect control is precisely because they can spread the transgenes rapidly by 'non-Mendelian' mean within a population, i.e., by replicating copies and jumping into genomes, including those of the mammalian hosts. Although each transposon has its own specific transposase enzyme that recognizes its terminal repeats, the enzyme can also interact with the terminal repeats of other transposons, and evidence suggest "extensive cross-talk among related but distinct transposon families" within a single eukaryotic genome.

It is disingenuous to claim that because only male mosquitoes are released that don't bite people or other mammals, the technique is "environmentally benign". First of all, the transgenic mosquitoes, both males and females, have to be mass-produced in the

[20] Professor Joe Cummins and Dr. Mae-Wan Ho, 2008. Terminator Mosquitoes to Control Dengue? Submitted to the FDA and EPA in the United States. 14/05/08

laboratory. In order for transgenic females, also carrying the dominant lethal in double dose, to propagate the line, they have to take blood meals from laboratory animals such as mice or rabbits, not to mention the odd lab worker, which gives plenty of opportunity for horizontal gene transfer. Second, the transgenic males have to be sorted from the females, and this takes place at the pupae stage, when males are generally smaller than females, but this may not be 100 percent accurate. Third, the tetracycline-dependence of the transgenic lines is not absolute. In the absence of tetracycline, 3 to 4 percent of transgenic progeny actually survive to adulthood.

It is obvious that transgene escape can readily occur. As Ho commented: “These artificial transposons are already aggressive genome invaders, and putting them into insects is to give them wings, as well as sharp mouthparts for efficient delivery to all plants and animals and their viruses.”

One cannot stress enough that horizontal gene transfer and recombination is the main highway to exotic disease agents.

The *piggyBac* inserts may also be mobilised by the transposase of *piggyBac* transposons already carried by Baculovirus (a common soil-borne insect virus) that infect insect cells, and this possibility has not been evaluated in the laboratory. Baculovirus not only carries *piggyBac* transposons, it has also been used in human gene therapy as it is capable of infecting human cells. It is indeed strange that the mobility and horizontal gene transfer of the *piggyBac* vector has not been thoroughly studied even though the activity of the vector is widely recognized.

The *piggyBac* transposon was discovered in cell cultures of the moth *Trichopulsia* , the cabbage looper, where it causes high mutation rates in the Baculovirus infecting the cells by jumping into its genes. The *piggyBac* itself is 2.5 kb long with 13 bp inverted terminal repeats. It has specificity for the base sequence TTAA (at which it inserts); the probability of this sequence occurring is (0.25) 4 or 0.4 percent in any stretch of DNA, where it can cause insertion mutations: disrupting and inactivating genes, or inappropriately activating genes. This transposon was later found to be active in a wide range of species, including

the fruit fly *Drosophila* , the mosquito transmitting yellow fever *A aegypti* , the medfly *Ceratitis capitata* , and the original host, the cabbage looper. The *piggyBac* vector gave high frequencies of transpositions, much higher than other transposon vectors in use, such as the *mariner* and *Hirmar*. The *piggyBac* transposon is also active in human and mouse cells, and in the mouse germline; and a version with minimal terminal repeats exhibited greater transposition activity in human cells than another, well-characterised hyperactive *Sleeping Beauty* transposon system widely used for preclinical gene therapy studies."

Source: ***http://www.i-sis.org.uk/Terminator_Mosquitoes_to_Control_Dengue.php***

According to an 'ex vector control staff', the dengue virus not only infects the salivary glands of the adult female *Aedes aegypii* mosquito but also the ovaries and eggs. When the eggs are laid, they are infected with dengue which persists through the larval and pupae stages. Consequently, when the adult females emerge, they are already dengue positive and transmit the virus on their first human bite.[21] Even if they mated with the GM male *Ae. aegypti* mosquito, the wild female mosquitoes will still be positive for dengue and transmit the disease throughout their adult life cycle. Further, the wild male mosquitoes from the dengue-infected eggs will also transmit the virus to any uninfected wild female mosquito that they mate with, thereby propagating the dengue virus to subsequent generations.

Given the risks factors in this project, a rigorous detailed risk analysis would be considered as an essential and necessary requirement. In his public response, the DG of Health, stated that the multi-sorting of the male GM from the female GM mosquitoes was '100 percent' accurate. On the potential impact of unintended release 'of a few (uninfected) females', it posed **'no significant risk'.**[22] He added that the GM mosquito release experiment was carefully thought through after four years of detailed, meticulous and stringent research by IMR.

[21] 'GM mosquito: Too many questions and no answers' November 17, 2010 Malaysiakini http://www.malaysiakini.com/letters/148492

[22] 'Study has been well researched'. *New Sunday Times* September 19, 2010 p20 http://www.nst.com.my/nst/articles/24gene/Article/

If the sorting of the male GM pupae from the female GM pupae was '100 percent' accurate, there should not be any unintended release in the first place. According to the DG, 'there are already far more wild female mosquitoes in the environment: the engineered females are shorter lived than wild ones, any offspring they produce would die, just as the released males.'

While acknowledging that female offspring do survive into adulthood, it was glossed over instead as the GM females will die anyway.

There was no mention that the survival rate of GM offspring into adulthood was three to four per cent. The figure of three to four per cent survival rate is highly significant considering the fact that one is dealing with an insect which is a vector for dengue and hence poses a serious threat to human health. Moreover, in the large numbers required for mosquito population suppression (in the millions), the three to four per cent survival rate results in many GM offspring survivors. As this data on survival rate may impact both human and animal health, was it factored in the risk assessment? In their decision to conduct the releases, were these studies taken into account?

As late as 2007, Oxitec and MOH would have known of the lab studies indicating the 3-4% survival rate. Oxitec Chief Scientific Officer Dr. L. Alphey was one of the co-authors of that research paper highlighting the unexpected survival results.[23] Why were these survival rates not made known to the public? Again, Oxitec has not been transparent. Or rather, again, has Oxitec something to hide?

Please note that the 3-4% unexpected survival was not reported directly by Oxitec or IMR in its public documents. It was first revealed in October 2010 by the head of GMAC to reporters at the height of concerns regarding the field releases. According to a SciDevNet report, Ahmad Parveez Ghulam Kadir, head of the Genetic Modification Advisory

[23] Phuc HK *et al*, 2007. Late-acting dominant lethal genetic systems and mosquito control 2007. BMC Biology 5: 11.; http://www.biomedcentral.com/content/pdf/1741-7007-5-11.pdf;
Atkinson MP *et al.* 2007. Analyzing the control of mosquito borne diseases by a dominant lethal genetic system. PNAS 104: 9540-5; http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1876161/

Committee (GMAC) – a technical advisory body to the NBB of the MNRE - said that the committee had been concerned that lab tests had shown that three per cent of the offspring of male GM mosquitoes and normal females actually survive into adulthood rather than dying as larvae as intended.[24]

The Advisory committee had also been worried that female GM mosquitoes might accidentally be released. The technicians separate the male from the female GM mosquitoes based on the size of the pupae — the stage after the larval stage — and is therefore not completely accurate. Because of this, Parveez said, the board has insisted that scientists sort through the pupae twice — first mechanically and then manually.

According to the same SciDevNet report[25], Ricarda Steinbrecher, a geneticist and co-director of EcoNexus, a UK-based non-profit research organisation, said that it is not clear how the offspring of the male GM mosquitoes survive into adulthood and do not die as 'programmed', but it raises the possibility that they could breed and pass on this — as yet unknown — mechanism for overcoming the lethality. She said, *"I would suggest that it is far too early for any open field releases. More data are needed from laboratory experiments. Furthermore, trials in field cages [large outdoor enclosures made from netting, i.e. confined field trials] are needed."*

However, previous MNRE and Oxitec responses to the public have been that the GM mosquitoes will not affect public health and safety or the eco-system!

Once again, Oxitec has not been truthful and transparent on important biosafety issues regarding the GM mosquitoes, and it seems the IMR has been complicit.

The proposed release should be stopped until biosafety issues are properly addressed.

[24] http://www.scidev.net/En/news/malaysia-to-release-gm-mosquitoes-into-the-wild.html
[25] Ibid. 19

5. Proper due process was not followed prior to GM mosquitoes release

GM mosquitoes importation, contained trials, and field releases are regulated nationally and internationally.

National level: Biosafety Act 2007[26]

Please take note that the NBB was only established recently in March 2010 under the Biosafety Act[27], but the Oxitec-IMR contained trials were done a few years ago, and were only approved administratively.

Thus, the contained trial conducted much earlier did not go through the NBB. The Biosafety Act 2007 requires the establishment of the NBB which will decide on all matters relating to the approval for release and import of living modified organisms.[28] The contained trial conducted much earlier remains controversial as it was contrary to the spirit of and the provisions of Malaysia's own Biosafety Act 2007. For example,

Section 22. Requirement for notification

(1) No person shall undertake any of the following activities without giving prior notification to the Board:

(a) exportation of living modified organisms;

(b) **contained use involving living modified organisms;**

(c) **importation of living modified organisms for purposes of undertaking a contained use activity.... .**

[26] http://www.biosafety.nre.gov.my/BiosafetyAct2007.shtml
[27] http://www.biosafety.nre.gov.my/act_nbb.shtml, and http://www.bt.com.bn/science-technology/2010/05/28/malaysia-sets-national-biosafety-board
[28] http://www-biosafety.nre.gov.my/biosafetyact2007.pdf

We are told that it took five years[29] before the GM mosquitoes were finally ready for release. Bearing in mind that the Biosafety Act 2007 only came into force in December 2009[30], what safeguards were in place during the unregulated years?

The Ministry of Health (MOH) was reported to have invited Oxitec in 2006, presumably with the GM mosquito eggs from the UK. For the last four years, the IMR has been working on the GM mosquito.[31] As such, the Ministry of Health's IMR was the body involved in the importation of the GM mosquito eggs or in other forms.

Section 12. Requirement for approval (Biosafety Act)
(1) No person shall undertake any release activity, or **any importation of living modified organisms**, or both without the prior approval of the Board.
(2) Any person who contravenes Subsection (1) commits on offence and shall, on conviction be liable ….

The MOH would have been involved in the process of drafting the Biosafety Act 2007. It would appear that the MOH was ready to import GM mosquitoes but the said Act was not in force. In which case, which was the regulatory authority responsible for the import process? Did the MOH notify the MNRE (under whose jurisdiction the Act falls) prior to its importation of the GM Aedes mosquito eggs? Did the MNRE approve? Under which process and criteria?

Since the NBB did not officially exist until March 2010, who or which body was responsible to ensure that the Biosafety Act was implemented? Was the Director General (DG) of Biosafety within the MNRE tasked with the responsibility? Under the Biosafety Act, the DG acts under the general authority and direction of the NBB. Since the NBB was only formed this year, under what laws or powers was the DG acting? Or were decisions simply made by administrative fiat bypassing legal requirements?

[29] MNRE says five years: MOH says four years.
[30] http://ictsd.org/i/news/biores/65569/
[31] Natalie Heng. Genetically-modified mosquitoes to fight dengue**.** *theSundaily* Tues 27 April 2010, http://www.thesundaily.com/article.cfm?id=46067

International level: Cartagena Biosafety Protocol[32]

The Cartagena Protocol on Biosafety (the Protocol) regulates the transboundary movements of living modified organisms (LMOs), which include GM mosquitoes. Therefore, the Protocol applies to the transboundary movement of GM mosquitoes between Parties (i.e. States which have ratified the Protocol) as well as between Parties and non-Parties to the Protocol.

Article 8 Notification (Cartagena Biosafety Protocol)
1. The Party of export shall notify, or require the exporter to ensure notification to, in writing, the competent national authority of the Party of import prior to the intentional transboundary movement of a living modified organism for release into the environment of the importing country.
2. The Party of export shall ensure that there is a legal requirement for the accuracy of information provided by the exporter.

Since the exporter was Oxitec, were the UK authorities aware that Oxitec was exporting its GM mosquitoes to Malaysia? Did Oxitec inform the UK government it was doing so? Did UK ensure that Oxitec follows the spirit and provisions of the Cartagena Biosafety Protocol? Did Oxitec or the UK inform the MNRE, 'the competent national authority'?

Oxitec is also legally bound under UK law to provide accurate information concerning the GM mosquito and its release. The Protocol also stipulates that the importing party (in this case, Malaysia and specifically MOH) is required in writing to inform the notifier, namely the UK government and the Biosafety Clearing House before it decides to release GM mosquitoes (**Article 10 paragraph 3**). Were these requirements carried out? Apparently not, as up to early December 2010, there are no details of the GM mosquitoes in the Biosafety Clearing House registries as already mentioned in an earlier section of this

[32] https://bch.cbd.int/protocol/

memorandum. Why was it put up on the BCH only on 14 December 2010[33] when clearance for the release was given much earlier? Why was there no documentation or mention on the BCH about the importation of LMOs from the UK to Malaysia in 2006 when IMR first started the research?

Similar concerns have been raised in the European Parliament on 14 December regarding Oxitec's activities in the Cayman Islands (Appendix 1).

Under the Advanced Informed Agreement Procedure, which applies to the environmental release of GM mosquitoes, the importing country shall ensure that risk assessments are carried out (**Article 15 paragraph 2**).

Article 16 paragraph 3 Risk Management:
'Each Party shall take appropriate measures to prevent unintentional transboundary movements of living modified organisms, including such measures as requiring a risk assessment to be carried out prior to the first release of a living modified organism'.

Thus, the risk assessment based on sound science should determine the likelihood of an unintentional transboundary movement of GM mosquitoes if they are to be released in the importing country. It also suggests that the importing country should require the exporting country to assess the likelihood that GM mosquitoes will cross borders unintentionally. It is obvious that if such an event is likely, the release should not be allowed.

Did the MNRE (or MOH) request Oxitec to do the risk assessment before it made the decision to import the GM mosquitoes?

Mosquitoes, natural or engineered, do not respect national borders. It is not possible for any country to control mosquitoes from crossing their borders. For instance, in the 1990s, the Asian tiger mosquito (*Aedes Albopictus*), a potential vector for dengue fever virus was introduced into the US in a shipment of rubber tyres imported from Asia. In fact, *Ae.*

[33] http://bch.cbd.int/database/record-v4.shtml?documentid=101481

aegypti is an invasive species introduced in the 1970s to Malaysia but is now part of the ecosystem.

What is the likelihood that any country can contain GM mosquitoes to remain within its borders in this age of air travel, and large scale movements of people and materials? For this reason, releasing a GM mosquito must be considered as a worldwide release which will potentially affect every nation on the planet.

In which case, there is every likelihood that an unintentional transboundary movement of GM mosquitoes will occur. **Article 17 paragraph 4 of the Protocol** states that the country where the environmental release occurred 'shall immediately consult the affected or potentially affected States to enable them to determine appropriate responses and initiate necessary action, including emergency measures.'

Thus as soon as the country of release knows of the possibility of GM mosquitoes crossing into other countries, they must provide information of this possibility to the concerned States. **Article 17 paragraph 3** says this information should include:

- characteristics of the GM mosquitoes
- estimated date of the release
- possible adverse effects to human health and the environment
- possible risk management measures.

Hence, were Malaysia's neighbouring countries such as Singapore, Indonesia and Thailand officially informed about the impending release? The MNRE had told the public that it 'used the guidelines developed for GM mosquitoes under the Cartagena Protocol on Biosafety.' Did it really?

The crucial questions remain: did the Malaysian authorities i.e. MNRE and MOH ensure that the import, contained trials and release of the GM mosquitoes conform to national and international laws, i.e. Malaysia's Biosafety Act 2007 and the Cartagena Biosafety Protocol?

6. Risk assessments (RA) lacking

In its scientific analysis of risk assessment concerning the GM mosquitoes field release, the MNRE had reportedly reviewed and taken into consideration the Environmental Impact Statement (EIS) by the United States Department of Agriculture on the release of insects carrying a dominant lethal gene (RIDL), i.e. the GM pink bollworm (developed by Oxitec) and the GM fruit fly as this RIDL technology is similar to that applied in the production of GM mosquitoes.[34]

However, the GM fruit flies and the GM pink bollworms are plant pests or agricultural pests that do not pose a threat to human health. In the words of a critic who was once involved in vector control: '*To imply that the same level of criteria should be applied to GM mosquitoes, a known human blood feeder and human disease vector vastly oversimplifies the safeguards that need to be considered*[35].'

Interestingly, a three-day workshop on the Risk Assessment of Transgenic Insects was held in Kuala Lumpur in November 2008 which was attended by 70 Malaysian scientists and decision-makers. This was the first part of a Capacity Building Project 'to develop national capacities in biosafety required to carry out risk assessments with appropriate scientific and technical skills'. This workshop was co-organised by MNRE, IMR and the Centre for Research in Biotechnology for Aquaculture, University of Malaysia, with support from the UNDP.

Participants assessed three case studies, namely the GM fruit flies, the GM pink bollworm and the GM Aedes mosquitoes. The GM Aedes mosquitoes case study was conducted as the risk assessment 'for a hypothetical large scale open field release in Peninsular Malaysia' and was only done on the last day of the workshop. The risk assessment for the GM mosquitoes which came out of the workshop was published in a paper entitled *Risk*

[34] Yamuna Perimalu, *GM mosquito: Stringent protocols in place.* Malaysiakini, 9 Nov. 2010. http://www.malaysiakini.com/letters/147700
[35] *GM mosquito: Too many questions and no answers*. Malaysiakini, 18 Nov. 2010. http://www.malaysiakini.com/letters/148492

Analysis of a hypothetical open field release of a self limiting transgenic Aedes aegypti strain to combat dengue.[36] The co-authors include Camilla J. Beech and S. Vasan, both of whom are from Oxitec Ltd.

According to GeneWatch UK[37], this risk assessment omits some serious potential risks and downplays others. For example, the workshop report:

- Describes the risk of an increase in the population of Asian Tiger mosquitoes (*Aedes albopictus*) as 'medium' but states that developing a genetically-modified *Aedes albopictus* strain should be considered as the response to this;
- Considers dead larvae only as a positive benefit to feeding fish;
- Omits the question of whether mosquito suppression will result in loss of human population immunity, although this is cited as a potential issue in other Oxitec-authored papers and described elsewhere as "*among the most important unanswered questions in dengue epidemiology and GMM* [Genetically Modified Mosquito]-*based control approaches*";
- Fails to consider the possibility that the dengue virus may evolve to become more virulent (which is considered a lower risk with population suppression approaches, such as Oxitec's, than with other GM approaches, but which is still at an early stage of study) (Appendix 2).

Since the Environmental Impact Statements (EIS) on GM bollworm and the GM fruit fly were the only two cases reviewed and cited by the MNRE, and no other risk assessment for GM mosquitoes was reported widely other than the paper from the workshop mentioned above, it appears that the paper is the **only** Risk Assessment conducted on the GM Aedes mosquito release which is in the public domain. In the absence of further information, this

[36] See: Beech *et al* (2009) *Risk Analysis of a hypothetical open field release of a self limiting transgenic Aedes aegypti strain to combat dengue*. Asia-Pacific Journal of Molecular Biology & Biotechnology 17(3):99-111). http://www.msmbb.org.my/apjmbb/html173/173g.htm , or http://www.msmbb.org.my/apjmbb/html173/173g.pdf

[37] Oxitec's genetically-modified mosquitoes: in the public interest? GeneWatch UK briefing. December 2010. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Oxitecbrief_fin.pdf

paper could be the sole basis of the approval of the GM mosquito field release, unless the Malaysian government categorically states otherwise.

As with the EIA done by the proponent and then reviewed by the EIA committee of the DOE, any RA done by the IMR and Oxitec should also be reviewed by an independent committee i.e. the NBB of the MNRE.

On 14 December 2010, the MNRE posted online the RA on the BCH website of the CBD.[38] In the posting, the date of the RA was 24 September 2010. However, in the RA report of the GMAC (which was also posted on the same BCH website), the submission date stated was 7 May 2010.[39] On page 4 of the 7 May RA report, the GMAC stated that it had earlier evaluated the RA and risk management plan submitted by the applicant. It appears that there is another RA report of which the date is unknown but should be earlier than the 7 May RA report. However, the actual RA report cannot be found in the public domain.

There are three dates for the RA i.e. 24 September 2010, 7 May 2010 and the undisclosed third. The NBB needs to clarify which was the real RA and make it available to the public. Or else, it should make all three RAs public.

In the 7 May RA report, the GMAC stated that a Risk Matrix was prepared where identified potential hazards, their likelihood and potential consequences were ranked by GMAC on a scale of 1 to 4. However, the ranked Risk Matrix itself is not made public. Neither is the rationale behind each ranking, which is a subjective ranking.

In view of the serious public health risks, the Risk Matrix and the rankings assigned by the GMAC members should be made available for evaluation by independent GM mosquito experts and public health experts. This is critical as the integrity of the RA is determined by the level of expertise involved. Please note that the GMAC members involved in the specific risk assessment areas are mainly not experts in animals or mosquitoes, rather their expertise are in plants (see Appendix 1 of GMAC RA report

[38] http://bch.cbd.int/database/record-v4.shtml?documentid=101481
[39] http://bch.cbd.int/database/record-v4.shtml?documentid=101480

dated 7 May 2010 and section 10 of this memorandum). How can plant experts effectively evaluate public health risks posed by animal disease vectors such as mosquitoes?

As well, there is a crucial biosafety issue which has not been addressed. According to the Biosafety Act 2007, an approval for this small-scale release of GM mosquitoes is deemed valid for other subsequent releases by the same applicant (IMR), including possibly large scale releases for similar field experiment purposes.

Section 17. Approval to be valid for subsequent release and import

'Where an approval has been granted to an approved person for a release activity involving any living modified organisms or products of such organisms or the importation of living modified organisms, such approval shall be valid for subsequent similar release activity involving the same living modified organisms or products of such organisms or importation involving the same living organisms undertaken by such approved person.'

The cumulative impacts of many such small-scale releases are not known as GM mosquitoes release is still novel. Hence, the long-term implications of such experiments and their cumulative impacts cannot be predicted. The implications for biosafety can be critical and far reaching. The government may be exposing the Malaysian population as well as that of the neighbouring countries to unnecessary health risks.

Hence, the many worrying concerns raised regarding the GM mosquito make it imperative that the Risk Assessment (RA), in line with the Precautionary Principle, be made public. Similar to the Environmental Impact Assessment (EIA) which is required by law, the detailed RA should be in the public domain. This is crucial as the people especially those in the release sites must know the details to make an informed decision.

7. GM mosquito field trials undermine UN CBD moratorium on Terminator technology

Similar to the Terminator seeds which are genetically modified to produce sterile seeds, GM mosquitoes are Terminator insects as they have been designed to produce sterile offspring. To date, no scientific data exists that can justify the field testing of Terminator technology nor are there any studies of potential ecological or socio-economic impacts. Indeed, there is no published information on this technology despite more than a decade of development.

Since 2000, the UN Convention on Biological Diversity (CBD) has imposed a de facto global moratorium on this technology. Terminator technology is referred to as Genetic Use Restriction Technologies (GURTs) by the UN. At the fifth meeting of the Conference of Parties (COP5) to the CBD, Decision V/5, section III para 23 clearly states that:

'… in the current absence of reliable data on genetic use restriction technologies, without which there is an inadequate basis on which to assess their potential risks, and in accordance with the precautionary approach, products incorporating such technologies ***should not be approved by Parties for field testing*** *until appropriate scientific data can justify such testing, and for commercial use until appropriate, authorized and strictly controlled scientific assessments with regard to, inter alia, their ecological and socio-economic impacts and any* ***adverse effects for*** *biological diversity, food security and* ***human health have been carried out in a transparent manner and the conditions for their safe and beneficial use validated.'***[40]

The moratorium on Terminator technology was upheld in 2006 at the 8th Conference of Parties (COP8) when there were attempts by Canada, Australia and New Zealand supported by the US government and the biotechnology industry to undermine it by insisting on a 'case-by-case risk assessment' of the technology. This clause would have potentially opened the door to field trials.

[40] http://www.cbd.int/decision/cop/?id=7147

Speaking on behalf of the G77 (a group of 130 developing nations) and China, Malaysia said that the reference to case-by-case risk assessment was 'clearly unacceptable' because it would potentially allow field tests. This would potentially undermine the de facto moratorium of the CBD. The CBD reaffirmed the moratorium and made it clear that any future research would only be conducted within the bounds of the moratorium: meaning no field trials.[41]

Leading up to COP8, over 500 organisations from 55 countries had called upon governments to ban Terminator technology. In India over half a million signatures called on the Prime Minister to maintain India's ban on Terminator technology and uphold the international moratorium. While the European Parliament overwhelmingly passed a resolution calling on European governments to uphold the CBD moratorium and reject the text on 'case by case'.

In its letter to the public in November 2010, MNRE had said 'that the approval process (regarding the terminator mosquito) is not as simple as it is made out to be … as approval is given on a **case by case basis.'**[42] Obviously, MNRE has not adhered to the UN CBD terminator technology moratorium.

Malaysia's decision to test the GM mosquitoes in the field in effect undermines the global moratorium on Terminator technology. Malaysia's decision is inconsistent with its international role where it is a key player in the CBD. In fact, Malaysia was responsible for introducing the biosafety issue in the CBD negotiations. Indeed, when countries worldwide are banning and rejecting Terminator technology, the GM 'terminator' mosquitoes release in Malaysia would be a step backwards for Malaysia.

8. Liability, redress and accountability issues

IMR-MOH's GM mosquito release is based on the success of the simulated contained field trials it conducted. This controlled experiment takes place in an artificial situation that

[41] Lim Li Lin SUNS#5992 – 23 March 2006 http://www.sunsonline.org
[42] Yamuna Perimula. *GM mosquito: Stringent protocols in place*. Malaysiakini. 9 Nov. 2010. http://www.malaysiakini.com/letters/147700

bears no relation to the real environment. As such there are many unknown factors making risk assessment difficult. Some of these concerns include the following:

- Once the GM *Aedes aegypti* mosquitoes are released into a new environment, they act as an invasive or exotic species would because they have new traits not found in other mosquito species. Furthermore, the natural *Ae. aegypti* is also an invasive species having been introduced into Malaysia. How the GM variety would affect the natural *Ae. aegypti* is currently not known.
- More seriously, the genes involved in the genetic engineering of the Aedes mosquito are not known. As the IMR has refused to release the information, the public are left guessing. How the genes work to kill the offspring of the GM male mosquito appear to be unclear and little understood. This should be investigated before any open releases are done, as they may have environmental or health risks.
- Genetic engineering technologies can give rise to unexpected and unintended effects in organisms. The genes may behave differently when they are transferred from one organism to another. If the unintended occurs in the environment, these releases would be impossible to monitor, contain or mitigate and they are irreversible. For example, the possibilities of horizontal gene transfer: this happens when the new genes engineered into the insects may 'jump' into other species causing unintended consequences to the ecosystem. Thus, the gene from the GM Aedes mosquito can be transferred to other species (possibly through bacteria) which could affect their reproduction given that the said gene causes offspring to die.
- Genetically modifying an Aedes mosquito which is a vector of a lethal disease may give rise to unexpected or new behaviours apart from the intended ones. For instance, the GM Aedes mosquito may become more virulent, and exhibit more aggressive mating or feeding behaviour, or its bite may have different effects on the host be it animal or human. Given that introducing a new gene is a random

process[43], each mosquito could potentially have different unintended behaviours from the next. These effects may have severe impacts on human and animal health.

- Another concern is that other insects, some probably more dangerous than *Ae aegypti*, might move into the ecological niche vacated by the mosquitoes. For instance, if the GM *Ae aegypti* is successful in suppressing wild populations, this could result in a surge of *Ae. albopictus* which transmits both dengue and chikugunya diseases.
- The IMR states that the mosquito larvae (produced after the GM males mate with females) will die if there is no tetracycline, an antibiotic, in the environment. Tetracycline is widely used in Malaysia for medical, agricultural, veterinary and livestock purposes. Therefore, if the eggs are laid in an area exposed to this antibiotic, its offspring may live and we may end up having the offspring of GM mosquitoes loose in the environment.
- The field trials will be done according to a Mark-Release-Capture technique. According to the NBB, this method entails very low risks. The GM mosquito has been given a gene that will create fluorescence. Presumably, since they glow in the dark, the GM mosquitoes will be easily recognisable. The capture plans include placing traps to recapture the GM mosquitoes and continuous daily monitoring of the traps until no marked mosquitoes are recaptured for three successive days. If marked mosquitoes are still being caught after one month, further trapping can be put in place.

  According to scientists, trappings are not guaranteed to be effective and the expression levels of the fluorescent marker to identify the GM mosquitoes may vary such that some GM mosquitoes may not be identifiable by fluorescence and hence escape detection.

- Furthermore fogging will be done. This is considered too optimistic as it does not take into account storms or strong winds that could spread the GM Aedes

[43] When genes are inserted into an insect's genome they are called transgenes. Transgenes are usually inserted using short sequences of DNA that randomly integrate into the insect's genome carrying the transgenes with them.

mosquitoes to a much wider area. The IMR plans to fog the areas with *Resigen*®. This pesticide contains *S-bioallethrin* and *permethrin*, both pyrethroids which have been linked to toxicity in humans including carcinogenicity, reproductive and developmental toxicity, neurotoxicity as well as acute effects like coughing, redness, burning sensation – pain in the eyes and skin, dizziness, headache, fatigue, nausea, listlessness, vomiting, epigastric pain, and muscular fasciculation (contraction and relaxation). These two chemicals can be inhaled or ingested directly or through water. *Permethrin* has also been found to have potential to be an endocrine disrupter.

Thus, fogging will expose the communities and the environment with these poisons.

Given all these unpredictable consequences and potential risks, the chances of things going wrong cannot be overstated. Why is the MOH paying Oxitec to test such a dangerous product on Malaysian soil? Why have we allowed ourselves to be guinea pigs for this dubious technology? What if the experiment does not go according to plan and something goes terribly wrong with the release? First and foremost, Oxitec will **not be** wholly liable as IMR-MOH is the Applicant for the release.

Moreover, the Biosafety Act is silent on the issue of liability and redress. Does it mean that Oxitec will get away scot free although it owns the patent rights to the GM mosquito? Who, how and where can the communities seek redress should any adverse health and environmental effects occur? Who will be held liable?

The MNRE says that liability issues and redress will be developed consistent with the recently adopted Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Biosafety Protocol.[44] This Supplementary Protocol is very different from the one developing countries, concerned scientists, farmers and NGOs had campaigned tirelessly for. The Supplementary Protocol is a set of administrative measures or rules that governments would need to make laws for and implement. In other words, the Supplementary Protocol places the responsibility on governments to seek redress from the

[44] https://bch.cbd.int/protocol/NKL_Protocol.shtml

person causing the damage; and for the government to take measures to clean up the environment in the event of biodiversity damage. Third parties who suffer damage as a result of the release of GMOs (like GM mosquitoes) will have to rely on domestic laws (tort) for redress. The deterrents and fines in the Biosafety Act are weak and paltry. Malaysia's laws on liability and redress would need to be more effective to ensure that redress and liability issues are sufficiently implemented.

In comparison, an international civil liability regime is one that establishes rules and procedures for redress for third parties for damage from GMOs. This international law on civil liability would have, among others, identified the persons liable for the damage caused; defined the scope of damage; provided for strict liability; addressed issues concerning access to justice; and jurisdiction of the courts.

This new Supplementary Protocol defines damage as an event that has happened (ipso facto) and it has to be 'measurable'. Damage has to be 'significant'. Ecological or health damages usually take years to materialise or happen, which means it will take as long to be detected, and remedied.

Given the pressing biosafety challenges that many countries are facing, the Supplementary Protocol does not offer much.

There are further issues that touch on the rights of the communities and other ethical considerations. Some of these include the following:

- Is there any commitment from the IMR, MOH and MNRE that in an unexpected adverse event or events, the communities will be compensated?
- Who will be accountable if deaths and or injury occur through GM mosquitoes, dengue or pesticide poisoning?
- Will the communities be compensated for the time, inconvenience and expenses incurred (if any) for participating in the field trials?
- In the event that opposition to the field trials grows, can the community withdraw their consent at this stage?

- In the absence of any international guidelines on the release of the GM mosquitoes, what are the national guidelines to monitor the field trials? Do they exist?
- What are the guidelines in place to ensure adequate protection for the communities? Have those who may be specifically at risk been identified? As children and the elderly may be at a higher risk, what measures have been put in place to protect them?
- Is there a mechanism in place to inform the public and the communities affected about the progress of the project?
- The Cartagena Biosafety Protocol requires each government to notify and consult other potentially affected governments should GMOs under their jurisdiction cross international borders due to release into the environment. Have the neighbouring countries been consulted to prepare for contingencies in case the GM mosquitoes cross national boundaries?

In view of the wide legal implications with regards to liability, redress and accountability, as well as the national and international laws involved, it is indeed worrying that there is no legal representative from the Attorney-General's Chambers sitting on the NBB and GMAC.

As well, the liability and redress issues affecting the local communities have to be clearly spelt out in the interests of justice and human rights.

9. Lack of transparency and effective public participation

When the NBB announced its decision to approve the GM mosquito field release, it was touted that this was the first time that public consultation was carried out to review the approval, whereby public concerns were addressed and taken into consideration.[45]

In the 30-day period for 'public consultation' which began in August 2010, the NBB received a total of 32 inputs from the public including scientists, academicians, private

[45] Bernama National Biosafety Board issues first certificate of approval for field trial of GM mosquitoes Oct 16, 2010 http://news.mylaunchpad.com.my/Home/Latest/Article?Key=9191172d-4565-4b38-afd7-e7552fd9f884

companies local and foreign and the NGO community. According to the press report, the majority of the inputs supported the field trials and only one third of them raised objections. In addition, we are told that residents of the field sites will be given an opportunity to seek clarification. However, the exact locations of the field trials and the schedule of the field trials were not reported in the public documents or announced to the public.

Based on the comments and letters in the media (both the online and printed media) from the public even after the 'public consultation' period had ended, it seems that the public were not fully aware of the GM mosquito release and that more time should have been given for public feedback.[46]

This public included individuals familiar with vector control and public health, academics and environmentalists. Their main concern - apart from the potential risks to environmental and human safety issues- was the lack of information concerning the GM release from the authorities. More than this, when both IMR and Oxitec were asked to comment on the public's concerns, they declined saying it was inappropriate as their 'application is now going through the final stages of regulatory scrutiny.'[47]

In fact, the IMR **refused to provide information** regarding the process, the transgene responsible for the dominant lethal trait, and details of the contained field trials.[48] The three-page IMR application for approval fact sheet does not contain substantive data on the technique used and the mode of action of the key gene that gives the lethal trait that kills the larvae produced by the GM male mosquito when it mates with wild females.[49] These have important bearing on environmental and health outcomes. According to a press

[46] 'GM Mosquito trial: A dangerous precedent' 13 Sep, 2010 Malaysiakini http://www.malaysiakini.com/letters/142539
[47] 'Landmark trial of GM anti-dengue mosquitoes' Aug 29, 2010 Malaysiakini http://www.malaysiakini.com/news/141397
[48] 'Proposed Release of GM Mosquitoes Ill advised' 9 September 2010 Sarojeni V. Rengam PAN AP http://www.gmwatch.eu/index.php?option=com_content&view=article&id=12472
[49] http://www.biosafety.nre.gov.my/consultation/fact%20sheet.pdf

report, a request to interview the IMR scientists involved in the GM mosquito experiment was also refused.[50]

The IMR as the applicant of the GM field release, and by extension the MOH, have been strangely silent in this entire matter. So far, it has been the MNRE, its Biosafety Department DG and the GMAC which have been the official spokespersons for the IMR. They have responded to public comments and the press where Oxitec, the company selling Malaysia the GM mosquitoes was also present.[51] This low profile policy is maintained even when IMR meets the media.

On 29 October, the Biosafety Department of MNRE held a Q&A session with the media which was posted on its website.[52] However, the online media was not represented. The resource people officially included the DG of the Biosafety Department and four others from the GMAC. The IMR was apparently not officially present. Among the questions were why Bentong and Alor Gajah were chosen as the release sites. For these questions, the DG invited a certain Dr Lee from the IMR to respond. Who this Dr Lee from the IMR is, remains a mystery.

The shroud of secrecy surrounding the project has not only caused great suspicions and alarm, it has created unease and anxiety among the Malaysian public. The undue haste in implementing the field trials has also been a subject of serious concern. In fact, foreign scientists like Ricarda Steinbrecher had said that the Malaysian trials must not proceed until a full, long term environmental assessment of the Cayman trials is performed.[53] Others like Assoc. Prof. Dr Maketab Mohamad, President of the Malaysian Nature Society had urged the government to have a moratorium on 'the release of all GMOs.[54] Another academic, Dr.

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[50] 'Mutant Mozzies' *The Sunday Star* (Fit4Life) November 21, 2010 pp SF2-3 http://thestar.com.my/health/story.asp?file=/2010/11/21/health/7435187&sec=health

[51] 'Mutant Mozzies' *The Sunday Star* (Fit4Life) November 21, 2010 pp SF2-3 http://thestar.com.my/health/story.asp?file=/2010/11/21/health/7435187&sec=health

[52] (http://www.biosafety.nre.gov.my/consultation/Question%20and%20Answer%20Session.pdf).

[53] 'GM mosquitoes: Wait for Cayman trials results' Nov 14, 2010 Malaysiakini http://www.malaysiakini.com/news/148188

[54] 'Buzz of GM mosquitoes still feared' *New Straits Times* October 31, 2010, p2 http://www.nst.com.my/nst/articles/02mmosa/Article/

Rosli Omar in calling for a halt to the experiment had warned that Malaysia is being used as a guinea pig.[55]

On 31st October, a press report quoted the MP for Alor Gajah Tan Sri Dr Fong Chan Onn who expressed concern over the possible health hazard posed by the field trials.[56] He said that 'Many residents from my constituency are worried over the release of GM mosquitoes in the area.'

The same report also cited the Malacca State health director Datuk Dr. Azmi Hashim who said that his office had yet to receive any instructions regarding the field release.

Please note that according to the NBB's Terms and conditions for the GM mosquito release, '*It is mandatory that the applicant through a public forum obtains prior consensus and approval from the inhabitants in the release sites …. .*'[57]

On 21st November, a press report quoting an official said that the Bentong Municipal Council had given the approval for the trial to go ahead.[58] However without public consensus the release cannot take place.

When it was publicly confirmed that Alor Gajah and Bentong will be locations for the GM mosquito release, the Biosafety Department DG had said the project depended on approval from the local authorities. 'If they do not agree, the department will be forced to look elsewhere.'[59] There is absolutely no mention about obtaining approval from the inhabitants in the release areas. It appears that it was more important to get the green light from the local councils. Even from the time the two GM mosquitoes field release sites were proposed, the people of Alor Gajah and Bentong were not consulted before the announcement was made. There was no public forum where members of the community could have raised their concerns or sought explanation regarding the GM mosquito release

[55] 'GM Mosquito trial: A dangerous precedent' 13 Sep, 2010 Malaysiakini http://www.malaysiakini.com/letters/142539
[56] Alison Lai, **'**Fong: Malaccans worried about health hazard posed by field trials', *The Sunday Star* October 31, 2010 pN14 http://thestar.com.my/news/story.asp?file=%2F2010%2F10%2F31%2Fnation%2F7334478&sec=nation
[57] http://www.biosafety.nre.gov.my/app_field/nbb_decision.shtml
[58] 'Exterminating Aedes' *The Sunday Star* 21 November 2010, SF1-3.
[59] Suganthi Suparmaniam, 'Alor Gajah Bentong picked', *New Straits Times* 30 October 2010 pp1, 6

from the authorities. Neither is the public informed as to what are the mechanisms whereby the communities at the release sites will be briefed, and how consensus and consent will be obtained. Hence, the IMR and MOH have failed to comply with the NBB's Terms and Conditions.

Although some 'feedback' was obtained[60], meaningful public participation was sadly lacking. Public announcements were made via small advertisements in two newspapers *Berita Harian* and the *New Straits Times* on the 5th and 19th August 2010; and on the Biosafety website inviting them to contribute their input during a 30-day 'public consultation' period. Only 32 inputs were received, including ten from overseas i.e. Singapore, Brazil, Norway, France, United Kingdom, USA, India, Belgium, Mali, and Canada. One does not know the proportion of the private sector, the scientific community, individuals and NGOs. Clearly, insufficient publicity and the short timeline had resulted in the poor public response. Public objections were ignored and there was little transparency as to how decisions to approve the GM mosquito field trials were made.

Openness in sharing information and effective feedback can only be achieved in a genuine open dialogue with all sectors of the interested public. Thus, public consultation include public hearings or forums, for the public to air their views and objections and the certainty that their inputs are considered in the process and decisions made. In the current process, one also has to be computer-savvy to receive information and to participate in the input process. MNRE says it has 'provided much information on alleged doubts and all vital information and the basis for which the decision' for the GM mosquito field trials was made as they are all available online. Again, 'for more details the public can contact' them online.[61]

Disseminating information through the internet is no substitute for information sharing and discussion at public meetings. Only then can prior informed dialogue with the public take place.

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[60] *Rumusan Isu-isu dari Konsultasi Awam.* http://www.biosafety.nre.gov.my/consultation/Isu-Isu Konsultasi Awam v2.pdf

[61] 'Strict approval process' *The Sun* Letter 26 November 2010 p14 http://www.sun2surf.com/article.cfm?id=54419

The lack of access to information has meant that the general public were not sufficiently informed about the project through the public media. However, the electronic media carried views and comments which were critical of the GM mosquito trials but this was not accessible to the majority of the Malaysian public. Although the printed media gave wide coverage to the issue (they were some letters published expressing caution and citing the potential dangers), most of the longer feature articles and reports were slanted in favour of the trials. In short, the reading public were told that if they do not want their loved ones to die, the GM mosquito was the solution.

No less than the Minister of Health had declared in a press conference that the government views the GM mosquito 'as one of the most efficient and fast ways of getting rid of the Aedes mosquito from our local environment'.[62] According to him, 'IMR had successfully and effectively wiped out Aedes mosquitoes in the lab and it is confident that it could help the nation fight the menace … if nothing is done many more are going to suffer and die from dengue.'[63] There was little space for contrarian views to be heard. In an interview on TV Astro Awani, it was reported that an IMR spokesperson even called environmentalists 'stupid'.[64]

Thus, there was hardly any balance in the way the whole issue was presented to the general public. It is apparent that from the outset, the authorities had made up their mind about the project and were going ahead with it despite public calls to be cautious and to take into account the precautionary approach based on valid concerns. That we are dealing with GM insects especially disease-carrying mosquitoes on which there are no agreed or finalised guidelines for biosafety assessment simply because there is very little information to go on, should be a push for the precautionary approach.

Malaysia should uphold transparency, rigorous scientific standards, the precautionary principle, justice and human rights, and ethical and lawful practices. Otherwise, we will be

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[62] SciDev Shiow Chin Tan, 2 November 2010
http://www.scidev.net/en/news/malaysia-to-release-gm-mosquitoes-into-the-wild.html
[63] Annie Freeda Cruez, 'It is for us to make the decision' *New Sunday Times* August 29, 2010 p2
[64] GM mosquito trial can wait' *The Sun* Letter November 16 2010 p11
http://www.sun2surf.com/article.cfm?id=54083

opening the floodgates for foreign corporations to dump in Malaysia other GM pests, crops, food, feed and processing in the future. What is at stake is the health of Malaysians and our neighbours, our environment and biological diversity.

The key objectives of the Cartagena Biosafety Protocol are to promote and protect biosafety and uphold the precautionary principle. The Protocol emphasises the importance of public awareness and participation in national decisions on GMOs.

Article 23 Public Awareness And Participation calls on governments to 'promote and facilitate public awareness, education and participation concerning the safe transfer, handling and use of' GMOs and the risks to human health. It urges governments 'to consult the public in the decision-making process regarding GMOs and shall make the results of such decisions available to the public.'

Thus, the Protocol calls for the public to be actively consulted on GMOs and biosafety. This includes individuals, communities and NGOs to be fully engaged and to enable the public to contribute to the final decisions taken by the government, thus promoting transparency and informed decision making.

Therefore, the Malaysian government should improve its public disclosure policies under the Biosafety Act 2007 to include transparency and effective public participation in line with the Protocol.

Genuine effective public participation allows all voices to be heard and considered, so that the public can make informed decisions. Human well being is at the core of public health and the government has a duty to respect, protect and fulfil the people's right to health. This extends beyond providing healthcare, health campaigns, more doctors, more hospitals and CT scans. It also means that the government's actions regarding public health must promote public trust and not instil public fear and uncertainty.

Therefore it has a duty to refrain from taking actions that can jeopardise the right to health of its citizens. In the context of dengue control and the GM mosquito trials, prevention of

epidemics extend to not to risk creating them. Hence our approach to epidemics should focus on engaging good sound science and epidemiology and not GM solutions.

10. The members of the GMAC[65] and the NBB[66]

According to the Biosafety Act 2007, the NBB acts on the advice of the GMAC.

Section 6 Establishment of the Genetic Modification Advisory Committee:

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(2) The function of the Advisory Committee is to provide scientific, technical and other relevant advice to the Minister or the Board

.

(5) Members of the Advisory Committee shall consist of experts from various sciences based and other relevant disciplines.

The GMAC comprises 13 members[67], all competent scientists and experts in their area of expertise. There are two members (including the Chairperson) from the MPOB (Malaysia Palm Oil Board); two from the MARDI (Malaysian Agricultural Research and Development Institute); and one from the MRB (Malaysian Rubber Board). The other members include a botanist, microbiologist, veterinarian, one member from the MOH Food Quality Control division, and one from the Department of Agriculture who has worked on seeds, and a representative from BiotechCorp who has worked with the Works Ministry for 32 years and IJM.

As can be seen most of the members have no expertise in mosquitoes, let alone GM mosquitoes. Two members may have some understanding of mosquitoes by virtue of their work in polio in the IMR and microbe analysis work in the UPM, but they may not necessarily be 'mosquito experts'.

[65] http://www.biosafety.nre.gov.my/Genetic Modification Advisory Committee.shtml
[66] http://www.biosafety.nre.gov.my/NationalBiosafetyBoard.shtml
[67] http://www.biosafety.nre.gov.my/Genetic%20Modification%20Advisory%20Committee.shtml

The DG of the Biosafety Department whose main function is to implement and enforce the Biosafety Act, has previously worked on the Clean Development Mechanism (CDM) issues. He was previously deputy undersecretary of the Forestry Division of the MNRE.

The NBB comprises ten members.[68] Three of them may possibly have GMO expertise. They include the Director of the IMR who also heads the Allergy and Immunology Research Centre; a professor who has worked extensively in the areas of microbiology, microbial genetics and paramyxoviruses (causes human and animal diseases); and a professor of molecular biology who specialises in tropical pathogens and biosafety regulations and risk assessment. However, the rest of the other NBB members are not experts in GM animals as they are from the fields of botany, management, public policy and administration. These are from the Sarawak Biodiversity Centre; the Department of Agriculture; Sabah Biodiversity Centre; Ministry of Plantation Industries and Commodities; Domestic Trade Cooperatives and Consumerism Ministry; Ministry of International Trade and Industry; and the Chair who is the Secretary General of the MNRE.

The lack of entomologists, independent vector control specialists, mosquito experts, geneticists and public health experts is worrying as the approval process of the GM mosquitoes trials appears to have been conducted without the relevant expertise. Further, the absence of lawyers familiar with the Cartagena Biosafety Protocol and Malaysia's Biosafety Act 2007 creates a vacuum on the legal side of the biosafety compliance component.

The heavy presence of plant experts and others on the GMAC and the NBB is no accident. The Biosafety Act 2007 in line with the Cartagena Protocol on Biosafety was formulated with GM crops for agriculture in mind. The text of the Protocol was crafted in the context of the laws of the World Trade Organisation (WTO) and the need for precaution in biotechnology and the protection of biodiversity. Thus, the Protocol deals primarily with GM seeds, trees, fish and farm products such as corn and other grains used for food, animal feed or processing. As such, Malaysia's Biosafety Act and its implementing bodies are focused on agricultural commodities.

[68] http://www.biosafety.nre.gov.my/NationalBiosafetyBoard.shtml

When GM mosquitoes related to public health were slotted for trials, both the GMAC and the NBB are handicapped. Unlike GM crops, the risks posed to the environment and human health by GM mosquitoes are far greater. Hence, the GMAC and the NBB should review the composition of its members to include expertise which can deal competently with the new emerging developments and potential hazards in biotechnology such as GM mosquitoes. Under the Biosafety Act 2007, Section 7, the Board and the GMAC are empowered to form committees and subcommittees to assist them.

Conclusion

This memorandum has outlined some of the serious ethical issues which need to be addressed before any field releases of the GM mosquitoes are allowed to take place. They include the one year delay by Oxitec in announcing the GM mosquito release in the Cayman Islands which have raised serious concerns among international biosafety experts; the three to four per cent unexpected survival of GM mosquito offspring which was not reported by Oxitec or the IMR in its public documents; and the import process and the contained trials carried out were approved in the absence of the NBB under the Biosafety Act 2007.

Additionally, the transboundary environmental release of GM mosquitoes is governed by the Cartagena Biosafety Protocol. As such Malaysia could have contravened national and international laws when it decided to import and release GM mosquitoes. Further, Malaysia could have broken the de facto UN moratorium on Terminator technology.

The absence of effective public participation and the shroud of secrecy surrounding the project, and the undue haste in implementing the field trials have caused unease and anxiety among Malaysians. Conflicts of interests of Oxitec have further fuelled distrust.

While acknowledging that dengue fever and malaria are serious mosquito-borne diseases that need to be controlled using safe measures, it is however very doubtful if the proposed release of GM mosquitoes to control dengue fever is proper and 100 per cent safe under the present dubious conditions. Several alternatives have been given.

In summary, there should be a moratorium on the planned release of these GM 'Terminator' mosquitoes.

Action proposals

In light of the issues raised above, we urge the following:

1. Actions related to the delay in Cayman Islands announcement, non-transparency and conflicts of interests by Oxitec

That the NBB and the Minister responsible for the enforcement of the Biosafety Act 2007 (also known as Act 678) use their powers under the Act to invoke, *inter alia*:

Section 5(e) - where so directed by the Minister, to perform or provide for the performance of the obligations arising from agreements, conventions or treaties relating to biosafety to which Malaysia is a party where such agreements, conventions or treaties relate to the purposes of this Act.

Section 18. Review of approval upon obtaining new information

(1) The Board may, in consultation with the Advisory Committee, review any approval at any time upon obtaining new information or evidence on the living modified organisms or products of such organisms in respect of which such approval was granted.

(2) If, on review of the approval, the Board is satisfied that there is a risk posed to human, plant or animal health, the environment or biological diversity, the Board may take any of the following actions .....

Section 33. Circumstances where Board may make further order on notification

(1) Notwithstanding the power of the Board to take any action under subsection 32(2), the Board may make a cessation order, impose any additional terms and conditions, order the approved person to make rectifications, or make any other order as the Board thinks fit in the interest of biosafety in the following circumstances:

(a) where there is a risk posed to human, plant or animal health, the environment or biological diversity;
(b) where the approved person fails to comply with any terms and conditions imposed on the notification;

(2) Where the Board makes a cessation order, the approved person shall cease all activities involving living modified organisms immediately and shall, within seven days from the date of the notification of the cessation, surrender the acknowledgement of the submission of notification issued under section 25 to the Board.

(3) Any approved person who contravenes any order made by the Board under subsection (1) or contravenes subsection (2) commits an offence and shall, on conviction, be liable.....

Section 67. Falsification, concealment and destruction of document

Any person, with intent to deceive, in respect of a document to be produced or submitted under any provision of this Act or any regulations made under this Act, who makes or causes to be made a false entry, omits to make, or causes to be omitted, any entry, or alters, abstracts, conceals or destroys, or causes to be altered, abstracted, concealed or destroyed, any entry, forges a document, or makes use of or hold in his possession a false document, purporting to be a valid document, alters any entry made in any document, or issues or uses a document which is false or incorrect, wholly or partially, or misleading, commits an offence and shall, on conviction, be liable ….

(a) where such person is an individual, to a fine not exceeding two hundred and fifty thousand ringgit or to imprisonment for a term not exceeding five years or to both; or

(b) where such person is a body corporate, to a fine not exceeding five hundred thousand ringgit.... .

2. Actions related to Terms and Conditions and Accountability, Liability and Redress

Due to the lack of information on the GM field release, the lack of open dialogue with the public and the flawed participatory process, we urge:

1. The Local Councils to withhold or withdraw the consent letter until the two communities at the release sites have been consulted and have given their prior informed consent for the GM mosquito release as stipulated in the Terms and Conditions by the NBB to the IMR.

2. Notwithstanding the above, the inhabitants at the release sites withhold their consent and approval until proper Liability and Redress issues and biosafety concerns are properly resolved.

3. That the NBB should make available on its website all the compliance documents, including the Risk Assessment (RA) and Risk Management (RM) reports, as well as a credible Emergency Response Plan related to this proposed GM mosquitoes release as per Sections 36, 37 and 60 of the Biosafety Act 2007.

4. That the NBB fully engage the public through open informed dialogue and hearings and that this process be made available to the public and the mass media.

5. That the media maintains balance in the GM release controversy availing both sides a fair reporting so that the public will be able to assess the issue independently.

6. That the GMAC and the NBB include in their panel independent experts in the areas of genetics, vector control, mosquitoes and public health.

7. That representatives from the AG's Chambers are included on the GMAC and the NBB to give their input on Malaysia's obligations to international treaties related to GMOs, as well as to national legislation.

8. In line with the Cartagena Biosafety Protocol to which Malaysia is party to, that the GMAC include members of the NGO community and independent experts to contribute to the consultative process.

3. Actions related to issues of 'due process' in the GM mosquito field release

Given the controversial background in which the import process and the contained trials were conducted, in the absence of the NBB and a national law on biosafety at the time, we urge Members of Parliament:

1. To ask the Minister for the MNRE and the Law Minister as the contained trials were conducted prior to the enactment of the Biosafety Act 2007 and the establishment of the NBB, who or which bodies gave consent for the trials, and what safeguards were in place. Is the relevant documentation available for public scrutiny?

2. To ask the Minister for the MNRE, and the Minister of the MOH as MOH was the body involved in the importation of the GM mosquito from Oxitec, was MNRE notified and consulted prior to the event? If so, is the relevant documentation available to the public?

3. To ask the Ministers of the MOH and the MNRE that under the Cartagena Biosafety Protocol, a risk assessment is required to determine the likelihood of an unintentional transboundary movement of GM mosquitoes if they are released in the importing country. Did the MOH or the MNRE request Oxitec to do the risk assessment before the decision was made to import the GM mosquito? If so, is the relevant documentation available to the public?

4. To ask the Ministers of the MOH and the MNRE, did MOH or MNRE inform the UK government and the Biosafety Clearing House in writing before it decided to import and release the GM mosquitoes? If so, is the relevant documentation available to the public?

5. To ask the Ministers of the MNRE and the MOH, were the neighbouring countries officially informed about the impending release? If so, is the relevant documentation available to the public?

6. To ask the Minister of the MNRE, what is the MNRE's position on the de facto UN moratorium on Terminator technology since Malaysia has imported GM mosquitoes which use Terminator technology?

–ends.

Abbreviations

BCH	Biosafety Clearing House
CBD	Convention on Biological Diversity
COP	Conference of the Parties
DOE	Department of Environment
EC	European Commission
EIA	Environmental Impact Assessment
GM	Genetically modified
GMAC	Genetic Modification Advisory Committee
GMOs	Genetically Modified Organisms
IMR	Institute for Medical Research
I-SIS	Institute of Science in Society
LMOs	Living Modified Organisms
MNCs	Multinational Corporations
MNRE	Ministry of Natural Resources and Environment
MOH	Ministry of Health
NBB	National Biosafety Board
NGOs	Non-governmental Organisations
RA	Risk Assessment
RIDL	Released Insects with a Dominant Lethal
RM	Risk Management
US EPA	US Environmental Protection Agency
US FDA	US Food and Drug Administration

Appendix I

PARLEMENT EUROPEEN

FICHE DE DEPOT D'UNE QUESTION PARLEMENTAIRE

Destinataire: CONSEIL El
COMMISSION

FR

QUESTIONS ORALES		QUESTIONS ECRITES	
Question orate avec debat (art. 115)	☐	Question 6crite (art. 117)	☒
Heure des Questions (art. 116)	☐	Question 6crite prioritaire (art. 117.4)	☐

AUTEUR(S): JOSE BOVE

OBJET: GMO Mosquito
(,a preciser)

TEXTS:
MEP Jose Bove asks DG environment whether shipments of genetically modified mosquito eggs by the Oxford-based biotechnology company Oxitec to Grand Cayman Island for use in experimental field trials in 2009 and 2010 were treated as exports of GMOs under Regulation (EC) No. 1946/2003 on the transboundary movements of genetically modified organisms, whether DG Environment received the relevant information from the exporter, made this information publicly available and reported this transfer to the secretariat or parties of the Cartagena Protocol.

Signature(s): Date:14/12/2010

Appendix II

Oxitec's genetically-modified mosquitoes: in the public interest?

by GeneWatch, UK

December 2010

The UK biotech company Oxitec has recently released 3 million genetically-modified (GM) male mosquitoes as part of an open release field experiment in the Cayman Islands.

The GM mosquitoes produced by Oxitec mate with wild female mosquitoes but are genetically engineered so that most of their offspring die before adulthood. This is intended to reduce the population of the released mosquito species, which is a carrier of the dengue virus, and hence to reduce the incidence of this tropical disease. However, there are many unanswered questions about the impacts of this technology and concerns about the process for approving these experiments.

Further open releases of Oxitec's GM mosquitoes are planned for Malaysia in December 2010.

This briefing provides background information about the company, its technology, and its recent and proposed experimental releases of GM mosquitoes.

Key findings are,

- Oxitec is losing approximately E1.7 million a year and owes E2.25 million to a Boston multi-millionaire investor which it is due to repay by 2013;
- Oxitec's business model assumes its developing country customers will be locked in to ongoing payments for repeated releases of millions of GM mosquitoes, allowing it to repay this loan and pay dividends to its investors, including Oxford University;
- The company's first open field trials of 3 million GM mosquitoes have been undertaken in the Cayman Islands (a British overseas Territory) - funded by UK charity the Wellcome Trust - without any consultation, public risk assessment, ethical oversight, or the consent of local people;
- Former UK science minister Lord Drayson and former President of the Royal Society Bob May have both acted as advisors to investors in the company (Oxford University Challenge Seed Fund and East Hill Management LLC respectively);
- The company has also received significant public subsidy, including more than £2.5 million in grants from the UK government-funded Biotechnology and Biological Sciences Research Council (BBSRC), mostly for joint projects with Oxford University;
- Oxitec has made misleading statements repeatedly in the media that its GM mosquitoes are sterile;
- Oxitec has played a key role in developing risk assessment processes for its own products and has omitted or downplayed some serious potential adverse effects of its technology in these risk assessment processes;

- Oxitec is developing a GM version of a second species of dengue-carrying mosquito (the Asian Tiger mosquito) because it is aware that this mosquito could occupy the ecological niche vacated by reductions in numbers of the first species it is targeting. This second species is more invasive and can carry more diseases;
- Decisions to invest in mass-production facilities for GM mosquitoes in Oxfordshire, speed Oxitec's products through regulatory processes, and begin experimental releases in open field trials have been taken by Oxitec's venture capital investors and grant funders in London, Oxford and Boston, rather than by the company's potential customers or people living in dengue-infected areas.

About Oxitec

Oxitec is a spin-out company from Oxford University, based at Milton Park in Oxfordshire. Isis Innovation (Oxford University's technology transfer arm) was responsible for helping to set up the company and assisting to obtain venture capital investment. In August 2008, Oxford Spin-out Equity Management (OSEM) was set up to manage the University's shareholdings in its spin-out companies and seek ways of maximising the value of its equity stakes: Oxitec is now part of its portfolio.

Oxitec's technology

Oxitec's patented technique for genetically modifying insects is known as RIDL (Release of Insects carrying a Dominant Lethal genetic system). These GM insects are intended to be used as a form of biological control to reduce natural populations of the target insect when released into the wild.

Oxitec has developed a number of products incorporating its RIDL technology. These include genetically-modified strains of the Yellow Fever mosquito (*Aedes aegypti*) and the Asian Tiger mosquito (*Aedes albopictus*): both of these species can transmit dengue fever. Oxitec also has novel strains of agricultural pest insects. A genetically-modified pink bollworm strain containing a heritable fluorescent marker and sterilised by exposure to radiation has been tested by the USDA in open field trials. However, pink bollworm containing the RIDL genetic trait has not yet been released in open trials. Genetically-modified Mediterranean fruit fly, Mexican fruit fly and olive fly have also been developed but have not yet been released.

The focus of this briefing is on Oxitec's lead strain of *Aedes aegypti*, OX513A, which has been released in open field trials in the Cayman Islands and is planned for release in field trials in Malaysia shortly.

The OX513A strain of the *Aedes aegypti* mosquito is genetically engineered to contain a red fluorescent marker and the RIDL 'conditional lethality' trait. Conditional lethality means that the mosquitoes have been engineered to be able to survive to adulthood only in the presence of tetracycline (an antibiotic used to treat bacterial infections such as urinary tract infections, chlamydia and acne). GM mosquitoes are bred to adulthood in the lab in the presence of the antibiotic and males are then released into the environment.

Before release, male and female mosquito pupae are separated mechanically. Sex separation by size sorting is expected to result in a population containing less than 1% females for release (less than 0.1% female if large males are also discarded). The intention is to release only males because they do not bite and transmit disease. The released males mate with wild females and their progeny die as late larvae or pupae. Continual releases of sufficient numbers of RIDL males are expected to reduce the mosquito population and hence the transmission of disease.

The late lethality means that genetically-modified larvae will compete with wild mosquito larvae for resources, adding to the expected reduction in population compared to the alternative approach of releasing irradiated insects (irradiation of adult insects causes the progeny to die as embryos and not form larvae). However, this means it is inaccurate to describe Oxitec's GM mosquitoes as sterile: they do reproduce but most of their progeny do not reach adulthood, usually dying at the late larvae/early pupae stage. Large numbers of dead GM mosquito larvae and pupae will result from a commercial-scale release programme and some genetically-modified pupae will also survive to adulthood (3 to 5% of the progeny of females which mate with GM males survive in Oxitec's laboratory experiments).

Preliminary computer modelling by Oxitec suggests that a ratio of about six RIDL mosquitoes to one wild adult female should be maintained to eradicate a population of *Aedes aegypti* mosquitoes over a time period of just over a year: however, these figures and the best strategy for timing and maintaining releases are highly uncertain. The female mosquito to human ratio in endemic areas is about ten to one and in this paper Oxitec suggests that 100 million to a billion GM mosquitoes should be stockpiled for a given project. Because mosquitoes reproduce continually, releases will need to be made frequently, probably weekly, to suppress the population. In other more recent papers, the company suggests that eradication is unlikely and that continual releases will be needed to maintain suppression (but not eradication) of the mosquito population.

The GM mosquitoes will be released into a complicated ecosystem, involving other mosquito species, predators and prey, the dengue virus, and the humans who are bitten. Because this system is poorly understood there remain unanswered questions about the impacts of the proposed releases, including:

- the numbers of GM mosquitoes that will be needed and the impacts of the large numbers of dead larvae and pupae and smaller number of surviving GM adults produced when they mate;
- whether other pests (especially the Asian Tiger mosquito *Aedes albopictus* which can transmit more diseases and is one of the world's most invasive species) will move into the ecological niche left by the reduced population;
- whether the dengue virus will evolve in response to become more virulently;
- whether there will be a reduction in herd immunity in the human population leading to an increase in disease transmission.

Fluctuations in the mosquito population will effect these complex interactions as will any loss of effectiveness of the RIDL system over time, or difficulties scaling-up to large-scale production.

Patents

The first patent relating to Oxitec's technology was filed in November 1999 by Isis Innovation, with Luke Alphey (Chief Scientific Officer at Oxitec) and Dean Thomas named as inventors (equivalent patents have been filed in a series of other countries including the US, Mexico and China). Six subsequent patents relating to GM insect technology have been filed by Oxitec with Luke Alphey named as inventor.' Five further Oxitec patents relate to methods for detecting gene sequences which also have wider applications (the named inventor on these applications is Fu Guoliang).

Oxitec's investors

Oxitec received £228,775 from the Oxford University Challenge Seed Fund (UCSF) in 2001 'at a critical time in its development'. The UCSF was set up following advice to the then New Labour government by biotech venture capitalist David Cooksey in 1988. Its role is to distribute investment from the UK Government, the Wellcome Trust and the Gatsby Charitable Foundation in order to help commercialise university research, with the aim of reinvigorating the UK economy. Oxitec was incorporated as a Private Limited Company in August 2002.

The company has raised venture capital in four funding rounds to date. In 2002 it received initial seed funding of £1.5 million from Oxford University and East Hill Management LLC of Boston. In June 2005 it secured a second round financing of £1.3 million from the original investors and Oxford Capital Partners (which invested £550,000). The company stated that the new funds would be used to progress its lead RIDL products (the Mediterranean Fruit Fly, the mosquito *Aedes aegypti*, and the Pink Bollworm) through regulatory programmes, and initiate research on new targets.25 In October 2007 Oxitec received £1.5m in a private investment round led by Oxford Capital Partners who invested Elm, the remaining £0.5 million coming from Landon Clay of East Hill Management. In December 2009 Oxitec closed a further investment round from both existing and new (unnamed) investors.28 The company's accounts state that this fundraising round secured an additional £1.7 million of equity investment.

In October 2010 Oxitec appointed Deloitte to assist in finding new equity capital to create increased production capacity for its GM mosquitoes for "a number of markets" in 2011.

Oxitec's grants

The UK government-funded Biotechnology and Biological Sciences Research Council (BBSRC) funded work undertaken by PhD students of Alphey's whilst he was still based at Oxford University covering: genes in fruit flies and insect population control through

transgenesis. Oxitec has since secured a series of awards and grants from the BBSRC totalling more than £2.5 million (the majority in collaboration with Oxford University).

In June 2005, Oxitec was awarded US$4.8m as part of an international consortium within the Grand Challenges for Global Health initiative, led by the Gates Foundation (in partnership with the Wellcome Trust, US Foundation for National Institutes of Health and Canadian Institutes for Health Research). The Wellcome Trust's Director, Sir Mark Walport, is also a member of the Grand Challenges for Global Health's Scientific Advisory Board.

In February 2010, Oxitec was granted a Translation Award from the UK charity the Wellcome Trust to begin open field trials of the OX513A *Aedes aegypti* genetically modified mosquito (including trials in South East Asia in 2010).

Oxitec's grants from the BBSRC are listed in full in the appendix. Other grants include:

- a three year World Health Organisation (WHO) grant from the Special Programme for Research and Training in Tropical Diseases (TDR) Innovative Vector Control Business Line, as part of an international consortium: the MosqGuide project (April 2008);
- a South East England Development Agency (SEEDA) Research and Development grant to develop the RIDL technology for the control of the Asian tiger mosquito, *Aedes albopictus* (August 2009);
- partnership in the Euros 8.5 million four year INFRAVEC (Research Capacity for the Implementation of Genetic Control of Mosquitoes) initiative under the EU's Framework 7 (FP7) research funding programme (September 2009).
- a grant from the UK government-funded Technology Strategy Board (TSB)'s 'Feasibility Studies for Technology-inspired Innovation' competition: to develop prototype equipment for use in mass-production of GM mosquitoes together with a manufacturing company (December 2008) (the TSB funds 75% the project cost, up to around £25,000)
- funding from the Technology Strategy Board (TSB) to develop RIDL technology in the tomato leaf miner, *Tuta absolute*, jointly with crop protection company BCP Certis (July 2010).

Oxitec's debts and business model

Oxitec's 2009 accounts state that the additional capital it raised in December 2009, together with a convertible loan facility of up to £846,000 secured in February 2010 was considered to be sufficient to fund the company's operations until at least the end of the first quarter of 2010. Footnote 12 to the accounts states: "During the course of the prior year, the company was provided with £1,500,000 unsecured loan facility by East Hill Venture Fund LP, a business which is controlled by LT Clay, a director of Oxitec Limited. This loan is repayable in 2013. At 31st December 2009, £1,500,000 (2008 £1,000,000) of this facility had been drawn down by the company. During the year the company was provided with and drew down a further £750,000 loan secured by way of

debenture over the company's assets. During the year interest charges of £131,800 (2008 £18,4O5) were accrued and added to the amount of the outstanding loans".

Oxitec made e loss in 2008 and 2009 of £1.7m a year: no dividends were paid to its investors. The company does not appear to have raised new capital since December 2009 and is presumably surviving based on the Wellcome Trust grant it secured to conduct the open field trials, as well as its other grants from the UK government-funded BBSRC and TSB, the Gates Foundation, EU and WHO/TDR.

David Bott of the UK Technology Strategy Board (TSB) reports a debate at Oxford Spin-out Equity Management (OSEM)'s conference on 22nd September 2009; "Oxitec, has a challenging business model. ...There was quite a debate about who the customer was and how to monetise the product - or is it a service?"

It is clear that Oxitec expects to gain income from continual releases of GM mosquitoes in large numbers in several partner countries and that it is attempting to speed its products through the regulatory process in order to repay its loan and start generating income for its venture capital investors. In order for its business model to be viable it will need to lock its customers - presumably developing country governments – into a system of repeated ongoing payments. Even if there are no adverse effects, releases of GM mosquitoes will need to be continual to avoid resurgence in the mosquito population.

Oxitec is now pioneering mass-rearing at its facility in Oxfordshire. This facility will serve as the primary production site and eggs produced in the UK will be shipped under permit to countries worldwide. The company states that local facilities will be established to increase numbers to meet the demands of the local release programmes.

The decisions to invest in these production facilities, speed Oxitec's products through regulatory processes, and begin experimental releases in open field trials have been taken by Oxitec's venture capital investors and grant funders in London, Oxford and Boston, rather than by the potential customers or people living in dengue-infected areas.

Friends in high places

The then UK science minister Lord Paul Drayson visited Isis Innovation on January 23rd 2009. During his visit he received an update from Oxitec. The company received its first payments from the Oxford University Challenge Seed Fund (UCSF) in 2001, when Drayson was a member of the UCSF board. Drayson's own biotech investments have been repeatedly criticised by the British press since it exposed that his own Oxford University spin-out company Powderject won a lucrative government contract shortly after he made a donation to the Labour Party (which was then in power). One article has suggested that he saved £1 million in tax by setting up a charity to manage his biotech investments.

Oxford Capital Partners offers investors a variety of tax benefits including 20% income tax relief (on investments up to £500,000); tax-free profits and exemption from inheritance tax (after two years). Names of its investors are not publicly available.

The Managing Member, co-founder, and Chairman of East Hill Management Company LLC is Boston multi-millionaire Landon T Clay. Clay is a member of the Oxitec Board. Bob May (now Lord May of Oxford) is listed by Business Week as a member of East Hill Management LLC's scientific advisory board but it also states he is President of the Royal Society (Britain's top scientific society), a position which he held from 2000-2005, so it is unclear when he joined the Board and whether he has now left. No current link with East Hill Management is declared in May's entry in the Lords' Register of Interests. May is a former Government Chief Scientist and a current member of the House of Lords. He is Professor Emeritus at the University of Oxford Zoology Department, where Oxitec's founder Luke Alphey is a Visiting Professor. Alphey was involved in preparing a 2001 Royal Society report on GM animals, which included a section on GM insects. Co-author Peter Goodfellow (then employed by GlaxoSmithKline) is also a Fellow of the Royal Society (FRS). He is married to Julia Goodfellow who was Chief Executive of the BBSRC from 2002 to 2007 and is also a member of the SEEDA Advisory Board (both bodies have given grants to Oxitec).

In November 2007 the World Economic Forum selected Oxitec as one of its Technology Pioneers: Alphey attended the Davos meeting in 2008 and 2009.

Oxitec is a customer of Ansteadbrook management consultancy, established in 2004 by Colin Ruscoe, former site manager at Syngenta Crop Protection. Ruscoe is Chairman of the British Crop Production Council. Ansteadbrook's other customers include Syntech Research (where Ruscoe is Director for Europe and Africa) and Syngenta Seeds. Syntech Research provides product development and regulatory services to the agricultural, biotechnology and food industries as well as government bodies and agricultural commodity suppliers. In 2005 Ruscoe joined the Executive and Scientific Committees of the Innovative Vector Control Consortium (IVCC) to develop commercial partnerships and apply grants (including $50m from Bill and Melinda Gates Foundation) to discover and deliver new chemical products and information systems for elimination of insect vectors of malaria and dengue. Oxitec obtained its consortium funding from the Grand Challenges in Global Health, led by the Gates Foundation, in 2005. The IVCC is also funding Syngenta to develop new insecticides for malaria mosquito control.

Oxitec's Chief Executive Officer, Hadyn Parry, and Regulatory Affairs Manager Camilla Beech are both former employees of Syngenta. Oxitec's Chief Executive Officer in Malaysia, Dr. Seshadri S. Vasan, is a former employee of the management consultancy firm McKinsey. Oxitec's business development manager for the Americas from December 2007 to February 2009, Joachim Prudencio Leao, lists his clients during this time on his CV as Fiocruz, Health Ministry, USP, Syngenta, Embrapa and Moscamed do Brasil, and one of his roles as facilitating the adoption of Oxitec's vector control technology in Brazil.

The full and referenced version of this document is posted on GeneWatch UK's website and is available for download here:
http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Oxitecbrief_fin.pdf