GeneWatch UK comments on Environmental Risk Assessment (ERA) of GM mosquitoes in Panama

February 2014

In February 2014, the Centro de Incidencia Ambiental de Panamá (CIAM) obtained a copy of the environmental risk assessment (ERA) produced by Panama's National Biosafety Commission for GMOs (CNB) for the project "*Transfer and evaluation of new technological alternatives for control of Aedea Aegypti through the use of transgenic mosquitoes in Panama*", dated 27th August 2012.[1] The risk assessment is accompanied by a covering letter from the Gorgas Institute[2] (dated 13th February 2014) and a number of official papers. These are:

- a letter from the President of the Sectoral Committee on Health Safety of GMOs (CSBS) to the President of the CNB (dated 10th January 2014)[3] enclosing;
- minutes of a 3 hour CSBS meeting held on 7th January 2014[4], at which it was concluded that there was no impediment to proceeding to the second phase of the experiments (open release of GM mosquitoes);
- Resolution CNB No. 01-2014 approving an experimental open release of GM mosquitoes in Nuevo Chorrillo (dated 14th January 2014)[5];
- Resolution CNB No. 027 approving the import by the Gorgas Institute of GM *Aedes aegypti* mosquitoes from UK company Oxitec for phase one of the experiments (contained use) and requesting the Institute and CSBS to report on progress and monitor the experiments (dated 15th January 2013).

The CNB ERA states (Section 6, page 5) that it is for contained use experiments involving Oxitec's OX513A strain of genetically modified mosquitoes. However, it also states that a second phase, involving open releases of GM mosquitoes into the environment, will be considered later, subject to permission from the CNB.

A list of frequently asked questions and Oxitec's responses[6] is also included with the documents, together with a public leaflet produced by the Gorgas Institute[7] and a description of public information activities in the area where open releases of GM mosquitoes are planned[8].

CIAM has asked GeneWatch UK to consider whether or not the CNB ERA provided meets the necessary standards for the CNB to reach an informed decision on whether or not to import GM mosquitoes for open release into the environment in Panama. A related question is whether or not local people have been provided with enough information to give their fully informed consent to the proposed experiments.

1. Standards required for the ERA

Under European law (Regulation (EC) No 1946/2003), Oxitec is required to provide an Environmental Risk Assessment (ERA) which meets European Union (EU) standards and to obtain consent from the importing country before it can export GM mosquito eggs for release into the environment overseas.[9] This Regulation implements the requirements of the Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity (CBD). Its aim is to protect human health and the environment from the possible adverse effects of the products of living genetically modified organisms (GMOs)[10].

The ERA provided by the exporter should meet the standards of EU rules on risk assessment contained in Directive 2001/18/EC[11]. For GMOs which are not plants, a list of issues that must be covered by the risk assessment is included in Annex II, D.1 of the Directive. Guidance published by the European Food Safety Authority (EFSA) outlines the

evidence that Oxitec would need to provide for its GM mosquitoes to be placed on the EU market (placing on the market means making available to third parties, whether in return for payment or free of charge).[12] Pages 73 to 107 of the EFSA Guidance provide details on the following specific areas of risk for GM insects:

- Persistence and invasiveness of GM insects, including vertical gene transfer (VGT);
- Horizontal gene transfer;
- Pathogens, infections and diseases;
- Interactions of GM insects with target organisms;
- Interactions of GM insects with non-target organisms (NTOs);
- Environmental impacts of the specific techniques used for the management of GM insects;
- Impacts of GM insects on human and animal health.

Directive 2001/18/EC also requires that the introduction of GMOs into the environment should be carried out according to the "step by step" principle. This means that the containment of GMOs is reduced and the scale of release increased gradually, step by step, but only if evaluation of the earlier steps in terms of protection of human health and the environment indicates that the next step can be taken.

According to documents obtained by GeneWatch UK under UK environmental information laws, Oxitec has not provided a risk assessment which meets EU standards to the Panamanian authorities.[13] Instead of providing its own ERA as part of the transboundary notification for shipment of GM mosquito eggs, as is required under EU law, Oxitec states that a risk assessment was undertaken by the CNB and CSBS, which the company claims that it has not seen.[14] According to press reports, the GM mosquito eggs for open release were due to be shipped out by Oxitec personnel in the week beginning 17th February 2014.[15] If this shipment has been made, it should have required an ERA meeting EU standards to be provided by the exporter (i.e. by Oxitec), followed by prior written express consent from the importer i.e. Panama (Regulation (EC) No 1946/2003).

In Panama, national legislation implements the requirements of the Cartagena Protocol on Biosafety (CPB).[16] Law 47 (9th July 1996), which pre-dates the CPB, covers the transboundary movement (import/export), contained use, intentional introduction into the environment, transit, risk assessment and management, handling, transport, packaging and identification of GMOs. Law 48 (8th August 2002) creates the CNB and Law 72 creates all other functions pursuant to the CPB. Resolution 046 of the Ministry of Health in 2012 creates the CSBS. Law 6 (22nd January 2002) covers issues of transparency and access to information.[17]

According to the CPB, the risk assessment provided by the exporting Party or exporter (under Article 8) is intended to inform a process which leads to a decision on whether or not to import the GMO (under Article 10). Risk assessments must be undertaken in accordance with Article 15 and the importer may require the exporter to carry out the risk assessment and to bear its cost. Parties are required to consult the public in the decision-making process, in accordance with their respective laws and regulations (Article 23) and to share information, including summaries of risk assessments, via the Biosafety Clearing House (Article 20).

Under the CPB, the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management has also produced Guidance on the Risk Assessment of Genetically Modified Mosquitoes.[18] It covers:

- Characterization of the living modified mosquito;
- Unintended effects on biological diversity (species, habitats, ecosystems, and ecosystem function and services);

- Vertical gene transfer;
- Horizontal gene transfer;
- Persistence of the transgene in the ecosystem;
- Evolutionary responses (especially in target mosquito vectors or pathogens of humans and animals);
- Unintentional transboundary movements;
- Risk management strategies;
- Related Issues.

In addition, relevant academic papers which discuss the risk assessment of GM insects, including GM mosquitoes, include Reeves et al. (2012)[19] and David et al. (2013)[20].

Below, we consider to what extent the ERA provided by the CNB (dated 27th August 2012) covers the information necessary to make a decision on import for open release of Oxitec's GM mosquitoes. We consider some of the information that would be required if the ERA were to meet EU standards, cover the issues identified by the AHTEG, and answer questions raised by academics and the CSBS. We focus on a number of key issues of most relevance to potential risks to human health. Because genetically modified mosquitoes are a new technology and the consequences of releasing them into the environment are poorly understood, other risks may arise that we have not identified below.

2. Analysis of the ERA

The first points to note are that:

1. The ERA that is legally required to be provided by Oxitec prior to shipment of GM mosquito eggs for open release is missing;
2. The CNB ERA states that it has been provided for contained use of GM mosquitoes (para 6, page 5).

It therefore appears unlikely that sufficient information has been provided to make a decision on import of GM mosquito eggs for open release or whether or not to allow open releases.

The CSBS meeting held on 7th January lists the following questions in relation to the second phase of the project (open release of GM mosquitoes):

1. Description and details of the release sites;
2. Detailed description of climatic conditions of the region where the GMO will be released;
3. Information on the type of barriers provided at the release site (geographical, biological and physical);
4. Time schedule and description of the activities;
5. Larval survey and level of infestation of *Aedes aegypti* in the communities in which the releases will take place;
6. Expanded evidence regarding approaches to the community (photos, meetings, surveys);
7. The 10 principle causes of illness and death with emphasis on fevers;
8. Taxonomical description of species related to the GMO in the region of study;
9. Specify and justify whether there is potential or not to cause a public health problem;
10. Specify possible interactions of the GMO with other species in the ecosystem;
11. The capacity to survive in the environment;
12. Susceptibility to contamination or infection;
13. Effects on non-target organisms;
14. Techniques, methods and elements of mitigation of possible risks;
15. Methods for protection of personnel (biosecurity).

Some information regarding items 1 and 6 are included in the document describing public information activities, however information on barriers (item 3) and the detailed time schedule and description of activities (item 4) is missing. The covering letter from the Gorgas Institute refers to monitoring with ovitraps in the area since 2011, however information from larval surveys (item 5) has not been included in the documents provided. Nor have the ten principle causes of illness and death (item 7) been listed. Items 8 to 15 are issues that should have been included in the risk assessment.

Some of these questions are considered in more detail below. We focus on the impact of the releases on other (non-target) mosquito populations; the impact on the target mosquito populations and on dengue fever; the release of biting female mosquitoes and the risks of biting and ingestion; the survival and spread of GM mosquitoes; and the transfer of traits to wild mosquitoes.

2.1. ***Impact on other (non-target) mosquito populations***

Releases of Oxitec's GM *Aedes aegypti* mosquitoes are intended to suppress the wild population of *Aedes aegypti*. Unlike removing breeding sites or using larvicides, this is a single-species approach which does not reduce populations of non-target species. One important question for the risk assessment is whether *Aedes albopictus* (Asian Tiger) mosquitoes, which also transmit dengue and several other viruses (including chikungunya), will increase in numbers and perhaps establish in new areas as a result of competitive displacement of one species by another.

The AHTEG Guidance includes, as an issue for consideration in the ERA: "*Whether, in the absence of the target mosquito, niche displacement by other disease vector species may occur, and if so, whether that can result in an increased incidence of the target disease or other diseases in humans or animals*" (page 47).

The EFSA Guidance states: "*Considering the aim and type of GM insect releases, and also accounting for possible accidental releases, potential impacts on NTO [non-target organisms] that may cause adverse effects include:…(b) a change in abundance or species composition of competitors (e.g. insects exploiting the same ecological niches) of GM insects and the ecological functions they provide*" (p.94) and adds "*Other pest species (e.g. secondary pests) might exploit the available resource and build up high populations which might have an adverse effect on the environment and on human health*" (p.98).

David et al. (2012) state that one issue for consideration is that: "*An initial increase (or decrease) in population size during the transitory state may suppress or displace (or release) a competitor species*".

The risk that numbers of *Aedes albopictus* could increase due to reduced competition for breeding sites and food is rated "medium" in the report of the NRE-UNDP-GEF workshop on Risk Assessment of Transgenic Insects in Malaysia in November 2008, as reported in a publication by Oxitec's Regulatory Affairs Manager, Camilla Beech, and others.[21]

In its draft risk assessment submitted to regulators in the USA Oxitec states (page 25): "*It is not clear to what extent Ae. albopictus could or would expand its range into areas currently dominated by Ae. aegypti but it is reasonable to expect a degree of such expansion if no countervailing activities are undertake*n".[22] Oxitec has also published a paper which uses computer modelling to show how *Aedes aegypti* and *Aedes albopictus* may interact.[23] The authors acknowledge that this could have important consequences for the persistence of disease.

The CSBS requested information on the effects on non-target organisms (item 13), and for the applicant to specify interactions with other organisms in the ecosystem (item 10), and to "*specify and justify whether there is potential or not to cause a public health problem*" (item 9). However, the CNB ERA does not mention *Aedes albopictus* at all (presumably because it was intended as a risk assessment for contained use only) and nor do any of the other materials provided. This means that the risk that *Aedes albopictus* mosquitoes increase in numbers or establish in new areas as a result of the proposed releases has not been considered. Nor has this risk been included in any of the public information materials that have been provided.

Benedict et al. (2007) report that *Ae. albopictus* (a native of Asia that has spread around the world) was established in Panama in 2002.[24] Researchers at Panama University have described *Aedes albopictus* as more dangerous than *Aedes aegypti* and regard it as a more invasive species which may be very difficult to tackle if it moves into an area.[25]

Oxitec frequently cites a review by Lambrechts et al. (2010) to support its claim that *Ae. albopictus* is a less effective vector of dengue than *Ae. aegypti*. However this paper also warns that it is not possible to predict the epidemiological outcome of competitive displacement of *Ae. aegypti* by *Ae. albopictus* and warns that vector status is a dynamic process that in the future could change in epidemiologically important ways.

In the Philippines, Duncombe et al. (2013)[26] suggest that increased numbers of *Ae. albopictus* mosquitoes in vegetative areas later in the wet season may extend spatial and temporal opportunities for dengue fever transmission, which would not be possible if *Ae. aegypti* were the sole vector. They also note that increasing co-circulation of dengue fever virus serotypes in human populations with specific herd immunity may increase the incidence of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which are more severe forms of dengue fever resulting from secondary infection with a different serotype. In Sri Lanka, Sirisena and Nordeen (2014) find that the role of *Ae. albopictus* has been underrated and this species is likely to play an important role in the maintenance and transmission of the virus.[27] The greater susceptibility of *Ae. albopictus* to infection is believed to have led to greater dengue virus adaptation, thus Sri Lanka as a whole may be at serious risk of multiple dengue fever/DHF outbreaks in the future with the evolution of new virus strains.

Recently, Grardet al. (2014) identified the presence of ZIKV (Zika virus) in the invasive mosquito *Aedes albopictus* in Gabon and raised the possibility of a new emerging threat to human health.[28]

It is clear that the risk of a spread or increase in *Ae. albopictus* should have been considered in the risk assessment as this could have serious negative implications for human health.

2.2. ***Impact on target mosquito population numbers and on dengue fever***

Oxitec has not assessed the possibilities that mosquito numbers in areas neighbouring the trials could increase as a result of the experiments; a rebound in mosquito numbers or cases of disease could occur when releases cease; or partial population suppression could increase the risk of the more severe form of the disease dengue hemorrhagic fever (DHF). These possibilities are risks to public health associated with undertaking trials in dengue-endemic areas.

The EFSA Guidance includes: "*Changes in TO* [target organism] *populations caused by the GM component of the releases (size, age structure, sex ratio, fertility, mortality) that may result in adverse effects leading to environmental harm*" (page 87) and "*Loss of immunity in*

the human population and reliance on continued long-term positive effects of vector suppression or replacement strategy" (page 109).

David et al. (2013) focus on malaria, but also note that: "*loss of acquired immunity may increase transmission… especially if vector suppression is only temporarily successful*".

The CSBS requested the applicant to "*specify and justify whether there is potential or not to cause a public health problem*" (item 9). However, none of the mechanisms through which attempts at population suppression could cause a public health problem have been included in the CNB ERA, presumably because this ERA was provided for contained use only.

Assessing these risks is extremely difficult due to the lack of public information. Oxitec has published the results of its population suppression trial in the Cayman Islands[29] but no results from its trials in Brazil (the only dengue-endemic country where population expression experiments have taken place so far). In Malaysia, only a small initial trial was conducted and experiments on population suppression did not take place before the trials were terminated.

In the Cayman Islands, Oxitec had to significantly increase its releases of GM mosquitoes, from the expected 3,150 males per hectare per week to about 14,000 per hectare per week, targeted on a small 16 hectare area, in order to achieve the observed population suppression effect. When local residents complained about the nuisance caused by the very large number of mosquitoes, Oxitec halved the number of adults released and deployed about 5,600 GM pupae in cages spaced 70-90m apart across the site three times a week. A recent paper, which fits a simple computer model of mosquito populations to the Cayman Islands data, predicts that releases of 7 million GM mosquitoes a week, in an initial phase, would be needed to suppress a population of 20,000 wild mosquitoes, followed by releases of 1.9 million GM mosquitoes a week for long-term suppression, if a mixture of pupal and adult releases are used, or 2.8 million a week if only adults are released.[30] The authors admit that in the real world, where mosquito populations are more complicated, higher numbers might be needed. This suggests that Oxitec's technology is not very effective and the prospects for sustained suppression of large mosquito populations may be very poor.

There are only two public sources of information about the population suppression effects of GM mosquitoes in Brazil. One is a report (the PAT report) from a workshop showing that a release ratio of *fifty-four* RIDL to one wild type male was used in the final phase of the experiments conducted in Brazil. The reported mating competitiveness was only 0.03 (3 in 100) on average and dropped to 0.012 (1.2 in 100) in the final phase.[31] More than half a million mosquitoes a week were produced during this late phase of the experiments and the releases were concentrated in a small area of houses in Itaberaba (Bahia), less than 500m by 200m. More recently, Oxitec has highlighted a claimed success in reducing the *Aedes aegypti* mosquito population in the village of Mandacaru in Bahia by 96%. The company has included one graph from this experiment in a booklet on its website, but no details have been published.[32] The releases were made in a village in the dry season in order to try to improve the chances of success.

The problem with poor efficacy is not only that it is a waste of money but also that it can give rise to unnecessary risks.

The first issue to consider is whether or not releases of GM mosquitoes could cause an increase in the numbers of mosquitoes in surrounding areas. This effect is predicted by some models for the release of sterile insects.[33] Oxitec's Cayman Islands' paper and its graph from Mandacaru both show increases in *Aedes aegypti* mosquitoes in the control area, as population suppression in the target area begins. In the Cayman Islands the control area was next to the target area for the releases, but for Mandacaru there is no public

information about the location of the control area. The number of mosquitoes trapped in the untreated area also increased in the final phase of the Itaberaba experiments according to the PAT report. Thus, there appears to be a real possibility that wild-type males, when swamped by very high releases of GM males, simply migrate to mate in the surrounding area, potentially increasing health risks for the people there. More information is needed to either confirm or rule out this possibility. Since Oxitec calculates population suppression based on the difference between the target area and the control area, it is possible that claims of significant drops in population partly reflect significant increases being caused elsewhere.

A second issue is whether there could be a rebound in mosquito numbers and/or cases of disease. The recently published model of Oxitec's releases in the Cayman Islands predicts a rebound in mosquito numbers when population suppression ceases. Another possibility is that there is a rebound in number of dengue cases increases due to loss of human immunity.[34,35,36] This is a possible mechanism through which the number of dengue cases could increase as a result of the experiments, especially if a reduction in the mosquito population cannot be sustained.

Perhaps the most important issue is whether cases of the more serious dengue hemorrhagic fever (DHF) might increase as a result of the experiments.

In its draft risk assessment submitted to regulators in the USA Oxitec states: "*It has been suggested that, in countries with very high transmission rates, reduction in transmission could increase the frequency of dengue hemorrhagic fever (DHF) even while decreasing the incidence of dengue fever*". The mechanism is a possible loss of cross-immunity to multiple serotypes of dengue.[37,38] Cross-immunity occurs at high frequency of biting but can reduce as the frequency of biting is reduced, leading to an increase in the frequency of DHF if the mosquito population is only partially suppressed. In its draft risk assessment for the USA, Oxitec dismisses this concern by making an unproven claim that the reduction in transmission will be well below the necessary level and pointing out that this concern is not relevant to the USA (where dengue fever is not endemic). However, this risk is highly relevant in Panama.

It is difficult to quantify this risk but it remains a matter of concern because: (i) no thresholds for dengue transmission or DHF transmission have been established in the proposed areas of release; (ii) only limited data (no data from Brazil) have been published regarding the claimed success of Oxitec's experiments to date; (iii) dengue and DHF have not been monitored during the Brazil experiments (and dengue is not endemic in the Cayman Islands); (iv) those results which are in the public domain suggest that the proposed releases will be inadequate to suppress the *Aedes aegypti* population sufficiently to avoid this risk.

The risk that partial or temporary suppression of the *Aedes aegypti* population could actually make the dengue problem worse is not discussed at all in the CNB ERA, presumably because this ERA was intended for contained use experiments only. However, partial or temporary suppression of *Aedes aegypti* populations could be extremely risky in dengue endemic areas and lead to harm to public health.

2.3. Release of biting females and risk of biting/ingestion of mosquitoes

One possible risk is that new proteins produced by the GM mosquitoes could have a toxic or allergic effect on humans or animals, if the GM mosquitoes are swallowed, or if female GM mosquitoes bite people or animals. Female GM mosquitoes can also spread disease. Although Oxitec intends to release only male GM mosquitoes a small proportion of females are expected to be released and some GM female larvae will also survive to adulthood.

The EFSA Guidance includes: "*Potential toxic effects of the new compound(s), their derived metabolic products and/or the GM insects to humans and animals, e.g. qualitative or quantitative change in the production of toxins by the GM insects when compared with their non-GM comparators*" and "*Potential allergenic effects of the new compound(s), their derived metabolic products and/or the GM insects to humans and animals*" (page 108)

The AHTEG Guidance also includes as an issue for consideration in the ERA: "*Whether the LM* [living modified] *mosquitoes are likely to affect other organisms with which they interact (e.g., predators of mosquitoes), and whether that could lead to an adverse effect (e.g., on the food chain)*".

Reeves et al. (2012) note that: "*there is the plausible concern that females could inject tTA into humans along with mosquito salivary gland fluids that are transferred as part of a normal bite*" and that "…*tTA-expressing females would occur in the environment in at least three circumstances: firstly, if heritable resistance to the RIDL construct was to arise in the wild; secondly, while the mechanical removal of females prior to release is highly effective, it is not 100%; and thirdly, when RIDL stocks are only partially sterile under field conditions. In fact, OX513A males are only partially sterile, and when they mate with wild females they will produce 2.8%–4.2% the normal number of eggs, half of which will be biting daughters*".

Oxitec has recently published figures on the number of biting female GM mosquitoes that are inadvertently released.[39] They report that female contamination is on average 0.02%. If correct, this would mean that 200 biting female GM mosquitoes are released in every million males. Current production of Oxitec's GM mosquitoes in Brazil is 4 million a week. In the Cayman Islands, mechanical sorting was less effective, leading to about 5,000 biting female mosquitoes in every million males (additional sorting was then performed by hand).[40]

Although no information on the scale of the releases has been included in the information provided, press reports state that the intention is to release 80,000 GM mosquitoes three times a week (240,000 a week) making a total of 5,760,000 in six months.[41] Using the figures from the sorting process in Brazil, this would mean 1152 biting female GM mosquitoes would be released during the first six months of the experiments. Poorer sorting could release many more and additional GM females will develop from any GM larvae that survive to adulthood.

In addition to the risk of being bitten, journalists have reported that in Brazil "…*it's impossible to talk during the liberation sessions without accidentally swallowing a few*…" due to the very large numbers of GM mosquitoes being released to try to swamp the wild population.[42]

It is therefore inevitable that some people and animals will get bitten by a GM mosquito and others will swallow or consume them.

Although figures for the expected number of biting female GM mosquitoes are not included in the CNB ERA, there are claims included that the proteins are not toxic. However, Oxitec has provided no data on the toxicity or potential allergenicity of the tTA protein expressed by its GM mosquitoes. Signs of toxicity[43] and neurotoxicity[44] have been reported in mice, yet these papers are not cited and Oxitec has provided no evidence that swallowing or being bitten by GM mosquitoes will not be harmful to humans or animals. In Spain, Oxitec has recently withdrawn an application to release GM olive flies while it undertakes further testing demanded by the regulators, including tests of toxicity to non-target species.[45]

2.4. **Survival and spread of GM mosquitoes**

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

The EFSA Guidance includes: "*Reduction in efficacy of the GM insect mediated trait that may result in adverse effects*".

The AHTEG Guidance requires consideration of evolutionary effects of concern "*that could result in a breakdown in the effectiveness of the technology and the resumption of previous disease levels*".

In the laboratory, 3% of the offspring of Oxitec's GM mosquitoes survive to adulthood, even in the absence of the antidote tetracycline.[46] When GM mosquitoes were fed cat food containing industrially farmed chicken, which contains the antibiotic tetracycline, the survival rate increased to 15-18%. Oxitec originally hid this information[47] but later admitted to an 18% survival rate of larvae fed on cat food in a published paper.[48]

Oxitec claims that this survival rate will not happen in the wild because the GM larvae will breed only in clean water. However, a number of studies have found that *Aedes aegypti* mosquitoes can breed in septic tanks where there can be high levels of contamination with antibiotics such as tetracycline. [49,50,51,52,53,54] *Ae. aegypti* also commonly live in areas where discarded takeaways are likely to contain meat contaminated with tetracycline.

The survival rate on tetracycline is mentioned in the frequently asked questions sheet provided by Oxitec, but is not included in the CNB ERA, presumably because this was produced to cover contained uses only.

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

Increased survival rates would reduce the effectiveness of any population suppression effect over time, increase the number of biting GM females, and potentially allow the GM mosquitoes to establish in the wild. These risks therefore need to be considered in the risk assessment.

2.5. Transfer of other traits to wild mosquitoes

Oxitec's GM mosquitoes have been developed from a non-native strain. In the Cayman Islands, the OX513A insertion in *Aedes aegypti* (originally developed from a Rockefeller strain[55]) was introgressed into a Mexico-derived genetic background by five generations of back-crossing;[56] it appears that this same strain was then used in Brazil and is probably the same strain intended to be released in Panama. Oxitec has not published any information about the origins of the Mexican strain and it does not appear to have tested the back-crossed strain for insecticide-resistance or disease transmission properties.

When Oxitec's GM mosquitoes breed with wild mosquitoes some of their other genetic characteristics will be passed on to the local wild mosquito population. Different strains of the same species are found in different places and some strains are more resistant to insecticides than others or better transmitters of disease (the four serotypes of the dengue virus and/or other viruses, such as Yellow Fever). The possible introduction of such traits needs to be considered. Harm to people's health can be increased if some serotypes or viruses can be transmitted more easily by the introduced strain than they were by the wild species already in the area, or if the strain is resistant to insecticides.

For comparison, in the UK, Oxitec has been prevented from releasing a GM diamondback moth (an agricultural pest) because of concerns about the use of a North American background strain, which is subject to controls under plant pest control regulations.[57]

3. Analysis of public information and engagement

It is widely recognised that fully informed consent from the public is needed for releases of genetically modified mosquitoes.[58,59]

Fully informed consent to medical research is a requirement of the World Medical Association's Helsinki Declaration (which covers the ethical responsibilities of medical professionals).[60] Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights. For example, all medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation (Article 17); the design and performance of each research study involving human subjects must be clearly described and justified in a research protocol (Article 22); the study must be approved by an ethics committee (Article 23) and participants must be fully informed about the study, including potential risks (Article 26).

In the absence of any published risk assessment, participants in the proposed GM mosquito experiments cannot be fully informed about the risks.

The leaflet and Frequently Asked Questions also fail to provide the necessary information about possible risks.

Reeves et al. (2012) provide a useful checklist (Table 1) of the kind of information that is necessary.

4. Conclusions

The following documents should be published and available for public consultation before open release trials of Oxitec's GM mosquitoes go ahead:

1. Oxitec's own ERA which is legally required to have been sent to Panama before GM mosquito eggs were exported for open release, under European law;
2. The ERA (if different) produced or considered by the CNB before making the decision to approve open release experiments: this must go beyond the CNB ERA supplied (dated 27th August 2012) which covers contained use applications only;
3. The results of Oxitec's experiments in Brazil, without which it is impossible to assess the risks of the proposed releases on public health in a dengue-endemic area;
4. The documented responses to the questions listed from the CSBS in its meeting on 7th January 2014.

A copy of the scientific protocol and ethical approval for the trial should also be provided, together with the permit provided for the import of GM mosquitoes for open release (consistent with the provisions of the CPB).

The CNB ERA provided is suitable for contained use only and does not meet the necessary international standards or requirements to properly assess the risks of releasing GM mosquitoes into the environment. Therefore, it does not provide an adequate basis for proceeding with the import and proposed release or for gaining the informed consent of local populations.

References

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