IV. Efficacy

Some commenters addressed the question of whether OX5034 would actually be efficacious in the field. Some of these commenters pointed to reports on the OX513A product that suggested that OX513A was not as efficacious as the company described to argue that additional efficacy testing was needed for OX5034. For example,

The Center for Food Safety (0344) and GeneWatch (0335) stated that:

> "Oxitec's letter to the EPA claims that effective mosquito control has been demonstrated with OX513A, but this contradicts the evidence outlined in the Cayman Islands, Panama and Brazil studies . . . . Further, it claims that effective mosquito control has also been shown for OX5034 in a trial in Brazil: however, there is no published evidence demonstrating this." (Center for Food Safety 0344 p. 15; GeneWatch 0335 p. 13)

GeneWatch UK (0335) concurred with the Center for Food Safety (0344) statement disputing Oxitec's claim that effective mosquito control was demonstrated with OX513A (p. 13).

The Center for Food Safety (0344) stated that:

> "To date, Oxitec has not established the efficacy of its technique for reducing *Aedes aegypti* populations, or the impact on relevant diseases (which may continue to be transmitted even by relatively small numbers of mosquitoes, including other species). Existing data from experiments elsewhere suggests the efficacy of this approach is poor (discussed further below) and there is no efficacy data for the United States. Further efficacy data would therefore certainly be needed before Oxitec could register its GE mosquitoes as a pesticide under 7 U.S.C. 136a. Based on the paucity of efficacy and other data Center for Food Safety opposes the granting of the experimental use permit, as further studies are first essential to establish that the proposed experimental use will not cause unreasonable adverse effects on the environment." (Center for Food Safety 0344 p. 14)

GeneWatch UK (0335) made the same comment, noting that:

> " . . . GeneWatch UK opposes the granting of the experimental use permit, as further studies are first essential to establish that the proposed experimental use will not cause unreasonable adverse effects on the environment. . . . (GeneWatch UK 0335 p.12)

L.M. Castro (0332) stated that:

> "A retrospective review of the environmental impact assessment that Oxitec presented to Brazilian authorities reveals that . . . the outcome of the experimental release of mosquitoes did not achieve the desired goals." (L.M. Castro 0332 p. 2)

Anonymous (0198) stated that:

> "Note that the so called success presented years ago by Oxitec in Brazil (Carvalho et al. PLoS NTD 2015) has been discussed via a re-analysis of their data in a peer-reviewed paper published in Lancet Global Health (Boete & Reeves, 2016)." (Anonymous 0198 p.1)

1. Comments Arguing That OX5034 is Not Likely to Be Efficacious Based on Previous Experience with OX513A

The Center for Food Safety (0344) and GeneWatch UK referred to previous testing with OX513A to argue that OX5034 built on the Oxitec RIDL technology is not likely to be successful. GeneWatch UK (0335) and the Center for Food Safety (0344) stated that:

> "Oxitec has conducted experimental open releases of its OX513A GE mosquitoes in the Cayman Islands, Malaysia, Brazil and Panama. In 2018, the Environmental Health Minister in the Cayman Islands confirmed that trials of Oxitec's GE mosquitoes there did not work and would be abandoned.[1] Oxitec's releases of GE mosquitoes in Panama and Malaysia ceased earlier, due to concerns about costs, effectiveness and risks. In Malaysia, trials were abandoned following a small open release experiment to measure flying distances and survival rates.[2] The health ministry concluded that "*the method was not practical besides involving high costs*".[3] In Panama, open release trials of Oxitec's GE mosquitoes were conducted in 2012 and then ceased, reportedly due to the high costs.[4] Proposed trials in other countries never actually took place. Oxitec notes that its former subsidiaries in Singapore, Mexico, Australia and Costa Rica are all now dormant.[5] Since its Cayman Island operations have now closed,[6] only the company's Brazilian office remains active. In Brazil, Oxitec released GE mosquitoes in

[1] Minister claims GM mosquitoes didn't work. *Cayman News*. 13 November 2018. https://caymannewsservice.com/2018/11/gm-mosquitoes-didnt-work

[2] Lacroix R, McKemey AR, Raduan N, Kwee Wee L, Hong Ming W, Guat Ney T, … Murad S (2012) Open Field Release of Genetically Engineered Sterile Male *Aedes aegypti* in Malaysia. *PLoS ONE* **7**(8), e42771. https://doi.org/10.1371/journal.pone.0042771

[3] No proposal to use GMO mosquitoes to combat dengue. *Free Malaysia Today*. 8 March 2015. http://www.freemalaysiatoday.com/category/nation/2015/03/08/no-proposal-to-use-gmo-mosquitoesto-combat-dengue/

[4] Proyecto de mosquito transgénico no arrancó. *Panamá América*. 1 November 2015. http://www.panamaamerica.com.pa/proyecto-de-mosquito-transgenico-no-arranco-998624

[5] Oxitec Limited. Annual Report and Financial Statements. Year ended 31 December 2017. https://beta.companieshouse.gov.uk/company/04512301/filing-history. p.22

[6] Oxitec packs up but evaluation not complete. *Cayman News Service*. 5 February 2019. https://caymannewsservice.com/2019/02/oxitec-evaluation-not-complete/

> Jacobina and Juazeiro in the state of Bahia, from 2011 to 2013. In 2016, Oxitec began larger-scale trials of its GE mosquitoes in Piracicaba, a city located in the state of Sao Paulo.[7] However, in 2018, Oxitec Brazil decided to close its GE mosquito factory in Piracicaba.[8] According to the company, the reason was the transition to the newer OX5034 version of its GE mosquitoes, which began to be released in a pilot project in Indaiatuba in the Campinas region, in mid-2018. In November 2018, Oxitec announced that in future it would only conduct trials with this new generation of GE insects.[9]" (GeneWatch UK 0335 p. 12; Center for Food Safety 0344 p. 13-14) [Emphasis in the original]

GeneWatch UK (0335) and the Center for Food Safety (0344) stated that:

> "Oxitec has repeatedly claimed that its experiments have been successful. In a brochure published in 2016, the company stated, "*Oxitec has developed a paradigm shift in mosquito control leading to unparalleled levels in the suppression of* Aedes aegypti*, the main vector for several of the world's most damaging viruses including zika, dengue and chikungunya*" and, "*In five separate efficacy trials across three different countries, releases of Oxitec OX513A mosquitoes led to a greater than 90% reduction in the local* Aedes aegypti *populations*".[10] However, these claims are not supported by the evidence.[11] For example, emails released as a result of Freedom of Information requests to the Cayman Islands' Mosquito Research and Control Unit (MRCU) reveal comments from scientists there with access to the data, which state, "*Whilst Oxitec and MRCU are making public statements proclaiming major reductions in the* Aedes aegypti *population in the treatment area the data I have seen does not support this.*"[12] and "*To date all the measures recorded have shown no significant reduction in the abundance of* Aedes aegypti *in the release area.*"[13] (GeneWatch UK 0335 p. 12-13;Center for Food Safety 0344 p. 15)[Emphasis in the original]

---

[7] Press Release: Oxitec expands vector control solution in Brazil. 31 May 2016. http://www.oxitec.com/oxitec-expands-vector-control-solution-brazil/

[8] Oxitec fecha fábrica e expõe fracasso da criação do mosquito transgênico. 27 July 2018. https://www.redebrasilatual.com.br/saude/2018/07/oxitec-fecha-fabrica-e-expoe-fracasso-da-criacaode-mosquito-transgenico

[9] Oxitec transitioning Friendly™ self-limiting mosquitoes to 2nd generation technology platform, paving way to new scalability, performance and cost breakthroughs. Oxitec Press Release. 28 November 2018. https://www.oxitec.com/2nd-generation-platform/

[10] Oxitec's vector control solution: A paradigm shift in vector control. Intrexon Corporation. 2016.

[11] Oxitec's GM insects: Failed in the Field? GeneWatch UK. 14 May 2018. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Failed_in_the_field_fin.pdf

[12] Email from MRCU scientist to Chief Officer, Ministry of Health, Environment, Culture and Housing (HECH), 4 April 2017. Communications between MRCU and Ministry. Released as a result of a Freedom of Information (FoI) request. 3 April 2018. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Communication_between_MRCU_and_Ministry_1.pdf

[13] Oxitec Project: Results to date. Attachment to email from MRCU scientist to Chief Officer, Ministry of Health, Environment, Culture and Housing (HECH), 4 April 2017. Communications between MRCU and Ministry. Released as a result of a Freedom of Information (FoI) request. 3 April 2018.

L.M. Castro (0332) stated that:

> "On the other hand, the potential benefits of this experiment are very limited. A study by Garziera et al[14] concluded that "the effectiveness of the release program began to break down after about 18 months, i.e., the population which had been greatly suppressed rebounded to nearly pre-release levels." (L.M. Castro 0331 p. 2)

GeneWatch UK (0335) and the Center for Food Safety (0344) stated that:

> "Oxitec's decision to stop releasing its OX513A mosquito and begin trials with a new female-killing version effectively confirms that its trials to date have all been a failure. In Brazil, commercial releases have never been approved by the Brazilian health authority ANVISA, which wants to see evidence of benefits to health before giving its approval, in line with recommendations from the World Health Organisation (WHO).[15],[16],[17] There is no commercial approval for releases because the company lacks any evidence of efficacy in tackling dengue or other diseases spread by this mosquito. (GeneWatch UK 0335 p. 13; Center for Food Safety 0344 p. 15)

GeneWatch UK (0335) and the Center for Food Safety (0344) stated that:

> "Further, GE mosquito production is extremely costly and there have been production problems. In 2014, the release of 300,000 GE mosquitoes in Panama was reported to have cost $620,000 (more than $2 per mosquito).[18] In the Cayman Islands, production issues included the release of a high percentage of female GE mosquitoes, high adult

---

http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Communication_between_MRCU_and_Ministry_1.pdf

[14] Garziera L., Pedrosa MC., de Souza FA., Gómez M., Moreira MB., Virginio JF., Capurro ML., Carvalho DO. 2017. Effect of interruption of over-flooding releases of transgenic mosquitoes over wild population of Aedes aegypti: two case studies in Brazil. *Entomologia Experimentalis et Applicata* 164:327–339. DOI: 10.1111/eea.12618.

[15] Anvisa decide que mosquito transgênico é objeto de regulação sanitaria [Anvisa decides that transgenic mosquitoes are subject to sanitary regulation]. ANVISA. 12 April 2016. http://portal.anvisa.gov.br/noticias/-/asset_publisher/FXrpx9qY7FbU/content/anvisa-decide-quemosquito-transgenico-e-objeto-de-regulacaosanitaria/219201/pop_up?_101_INSTANCE_FXrpx9qY7FbU_viewMode=print&_101_INSTANCE_FXrpx9qY7FbU_languageId=en_US

[16] Anvisa decide que mosquito transgênico é objeto de regulação sanitaria. REDE Brasil Actual. 12 April 2016. http://www.redebrasilatual.com.br/saude/2016/04/anvisa-decide-que-mosquito-transgenico-eobjeto-de-regulacao-sanitaria-7405.html

[17] WHO (2016) Mosquito (vector) control emergency response and preparedness for Zika virus.18 March. http://www.who.int/neglected_diseases/news/mosquito_vector_control_response/en/

[18] Liberados 300 mil mosquitos transgenicos [In Spanish]. TVN-2. 9 May 2014. http://www.tvn-2.com/nacionales/Liberados-mil-mosquitos-transgenicos_0_3931106958.html

and larval mortality, and mould in the rearing unit.[19] " (GeneWatch UK 0335 p. 13; Center for Food Safety 0344 p. 15)

The Florida Keys Environmental Coalition (0331) arguing that the numbers posted for suppression in the trials in the Caymans and Brazil remain in strong dispute, stated that:

> "In the Cayman to the chagrin and protest of Dr Wheeler and his staff, the government published a 62% suppression level after over a year of the trial, yet Oxitec posted 96% on their website to this very day. In Brazil the estimated from Danillo Carvalho, Univ of Sao Paulo, suggest suppression in the range of 60 – 70%, but Oxitec claims 92%." (Florida Keys Environmental Coalition 0331 p. 2)

The Center for Food Safety (0335) and GeneWatch UK (0335) stated that studies necessary to fully evaluate OX5034 include:

> "Published confirmation and independent verification of Oxitec's claim that its trial of OX5034 in Brazil has been successful . . . ." (Center for Food Safety 0344 p. 18; GeneWatch UK 0335 p. 17)

Anonymous (0005) stated that:

> "The applicant failed to submit any certified data arising out from the use of this product in Brazil, Panama and elsewhere; indicating the effectiveness and long term safety to humans, and other species. Therefore, EPA should request such certified data in order to seriously consider the application." (Anonymous 0005 p. 1)

W. Jordan and A. Jones (0327) stated that:

> "The EUP application should contain, and EPA should assess, all specific information – including the design of any efficacy assessments and the results obtained – used by the applicant to conclude that the GE mosquitoes were 'successfully deployed' in other areas (Cayman Islands, Brazil, Panama)." (W. Jordan and A. Jones 0327 p. 1-2)

2. <u>Comments Suggesting Alternative Approaches</u>

Commenter E. Young (0030) stated that:

Commented [WK1]: BPPD Response: BPPD understands that efficacy has varied based on assessments conducted in other countries. The purpose of the experimental use permit is to address such concerns and measure the efficacy of OX5034 in the United States. While there may be evidence demonstrating that this and similar products have had limited efficacy, that is not a reason not to issue an EUP.

Commented [WK2]: BPPD Response: BPPD has conducted a rigorous human health and environmental risk assessment

Commented [WK3]: BPPD Response: BPPD may accept data from other countries to support the Section 3 commercialization registration, when and if, OX5034 is submitted for review.

[19] Email from MRCU scientist to colleague, 15 September 2017. Communications between MRCU staff. Released as a result of a Freedom of Information (FoI) request. 3 April 2018. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Communication_between_MRCU_staff.pdf

"I don't think GM mosquitoes will be effective - just release enough sterilized males (that don't bite) to compete with wild type for females. It worked with the screw fly and will work with mosquitoes. No need to introduce new genes." (E. Young 0030 p. 1)

Commented [WK4]: BPPD Response: Mosquito control is a wicked problem that has been abated by techniques that have been effective for other pest species (i.e., screw fly). Further, it is not in the purview of EPA to deny a product registration based only on the existence of other control options being available.

Anonymous (0219) suggested that:

"Killing the carrier will not get rid of the viruses. They will find a different mosquito or a tick or some other way to spread and survive. And now we're left with a GM mosquito with no natural predators that may be even more dangerous than the one that was eliminated. Kill the virus where it breeds and not the carrier." (Anonymous 0219 p. 1)

Commented [WK5]: BPPD Response: OX5034 is not meant to eliminate mosquitoes completely. In addition, the viruses transmitted by mosquitos are tightly co-evolved with the insect species. It is unlikely that the viruses will transfer to a new host if mosquitos are eliminated.

3. Potential Effect of Integrated Pest Management on OX5034 Efficiency

GeneWatch UK (0335) and the Center for Food Safety (0344) stated that:

"The role of Oxitec's GE mosquitoes in Integrated Pest Management (IPM) is also highly questionable. Continuing to use traditional control methods for mosquitoes (adulticides and larvicides) could further limit the effectiveness of Oxitec's technology by killing the GE males before they mate with the wild female mosquitoes, or the larvae before they survive to reproduce the trait and spread it through the wild population. Moreover, since there is little data regarding the effectiveness of existing measures, it is hard to see how the claimed benefits of adding GE mosquito releases to existing measures will be evaluated. On the other hand, failure to use existing control methods (if and when they are effective) in order to allow GE mosquito releases to take place, may put people at unnecessary risk of dengue or other diseases, or simply add to the nuisance of mosquito bites, perhaps with negative impacts on tourism or quality of life." (GeneWatch UK 0335 p. 13; Center for Food Safety 0344 p. 15)

Commented [WK6]: It is not within EPA's purview to assess the efficacy of OX5034 in conjunction with other conventional overspray programs.

4. Comments Arguing That There Are Other Alternative Approaches

The Florida Keys Environmental Coalition (0331) argued that EPA that if an emergency does arise:

" . . . Wolbachia infected male releases, represent a more mature, lower concern Sterile Insect Technique (SIT) product with more effectivity, availability and greater product depth that would also be able to prevent any potential back filling of Aedes

> Albopictus, which was clearly demonstrated in the Panama trials by Oxitec." (Flroida Keys Environmental Coalition 0331 p. 3)

Commented [WK7]: I don't understand what the question is here… that they like Wolbachia better? I don't think we have to respond to that.

Anonymous (0329) stated that:

> "GM mosquitoes are riskier than current control methods." (Anonymous 0329 p. 1)

Commented [WK8]: BPPD has conducted a rigorous human health and environmental risk assessment

T. Ritchie (0223) stated that:

> "We need to do better than this, like China has with irradiating mosquitoes. Why can't we try this method first?
> https://www.the-scientist.com/news-opinion/combination-strategy-nearly-eliminates-invasive-mosquitoes-in-field-66165
> Let's try this instead, please? [HYPERLINK "https://mosquitomate.com/?v=3.0"]" (T. Ritchie 0223 p. 2)

Arguing that other control methods might be preferable, Friends of the Earth (0342) pointed out that:

> "Oxitec's intention of elimination targets one vector, whereas other vector control methods target breeding grounds for many vectors, either through removing breeding sites in an area or by using repellents for many species." (Friends of the Earth 0342 p. 3)

Commented [WK9]: It is not within EPA's purview to assess the efficacy of OX5034 in conjunction with other conventional overspray programs.

5. <u>Comments Arguing That OX5034 is Efficacious</u>

N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341) stated that:

> "The 2nd generation mosquito has been successfully tested in Brazil. In partnership with the municipal vector control authorities in the city of Indaiatuba, the pilot project demonstrated the new strain's effectiveness in suppressing populations of the *Aedes aegypti* mosquito – the primary vector of dengue, Zika, chikungunya and yellow fever – in four densely populated urban communities across the city. Post-trial monitoring has also confirmed that the self-limiting gene does indeed decline and disappear post-release." (N. Rose 0341 p. 1)

N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341) added that:

> "Releases of Oxitec's OX5034 *Aedes aegypti* were conducted in four separate communities under approval issued by Brazil's national biosafety authority, CTNBio, during a year-long trial starting in May 2018. The trial was designed to test a number of performance features of the 2nd Generation OX5034 *Aedes aegypti*, including the

> performance outcomes generated by the use of two different mosquito release rate levels in dense urban environments. Abundance of wild *Aedes aegypti* was monitored before and during the release program to allow for an accurate evaluation of the trial's impact. Wild *Aedes aegypti* numbers were kept at low levels throughout the high season in all treated neighbourhoods, whereas populations in areas untreated by Oxitec's OX5034 *Aedes aegypti* rose as normal." (N. Rose 0341 p. 2)

N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341) further stated that:

> "Relative to the untreated control area, releases of OX5034 male mosquitoes achieved an average of 89% peak suppression across two communities treated with a low release rate of mosquitoes and an average of 93% across two communities treated with a higher release rate. The optimal suppression observed was in one community wherein a 96% peak suppression with the high release rate over a four-week period was achieved. ("Peak suppression" is measured using the highest sustained suppression over a four-week period in an Oxitec-treated site when compared to a control site untreated by Oxitec mosquitoes for the same period of time. This measures the intervention's sustained suppression effect over time, which is a more accurate measure than selecting suppression results from a single day or week.)" (N. Rose 0341 p. 2)

N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341), referring to a paper by Garziera et al[NOTEREF _Ref31302649 \h * MERGEFORMAT] referenced in the Evan et al[NOTEREF _Ref30598723 \h * MERGEFORMAT] paper to suggest that the effectiveness of the OX513A release program began to break down after 18 months, stated that:

> "In fact, (Garziera et al., 2017)[NOTEREF _Ref31302649 \h * MERGEFORMAT] states that mosquito populations in the two treated areas remained suppressed for some time after OX513A released ceased: "*The mosquito population in Juazeiro (Mandacaru) remained suppressed for 17 weeks after the release interruption, whereas in Jacobina (Pedra Branca) suppression lasted 32 weeks*." There is no evidence in (Garziera et al., 2017)[NOTEREF _Ref31302649 \h * MERGEFORMAT] to support speculation that the program started to break down while OX513A mosquito releases were under way." (N. Rose 0341 p. 5)[Footnote inserted][Emphasis in the original]

N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341) pointing to the Evans et al[NOTEREF _Ref30598723 \h * MERGEFORMAT] paper stated that:

> "The paper reports that OX513A releases successfully reduced the wild mosquito population, as the mosquito was designed to do." (N. Rose 0341 p. 3)

Addressing the comments that referred to gene drives, N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341) disputed any suggestion that OX5034 might be a gene drive:

> "Oxitec's self-limiting technology works in the opposite way from gene drive. Oxitec's 2nd Generation mosquitoes carry two copies of the self-limiting gene. When Oxitec's males mate with wild females, the self-limiting gene persists only in males. Females that inherit the gene cannot survive to reproduce. Therefore, the self-limiting gene gradually declines in the population gene pool and cannot persist, enabling potential population suppression across multiple generations before the gene is eliminated from the environment." (N. Rose 0341 p. 7)

N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341) explained that:

> "Gene drive is a genetic engineering technology that propagates genes throughout a population without any off-switch. As a result, the gene drive insertion in the genome will re-occur in each individual insect that inherits one copy of the modification and one copy of the wild-type gene. The gene drive gene is thereby designed to convert wild-type (unmodified) counterparts into gene drive too. Therefore, these systems are designed to eventually become established or fixed in the population. Gene drive thus spreads and persists in the environment." (N. Rose 0341 p. 7)

N. Rose, Head of Regulatory Science, Oxitec, Ltd., (0341) further explained that:

> "By releasing enough self-limiting male insects over a sustained period to mate with pest females and thereby reducing the number of female progeny, the pest population is suppressed. In contrast to the design of gene drive technologies, if releases of Oxitec males cease, the pest population can recover. As female carriers of the self-limiting gene cannot survive to reproduce, the self-limiting gene also cannot establish or become invasive in the wild." (N. Rose 0341 p. 7)

Commenter P.L. Goodman (0068), noting that "two of the three SIT techniques are very labor intensive and are probably expensive in their application since they typically involve releasing adult male mosquitoes", stated that:

> "Based on the application provided by Oxitec for their second generation genetically engineered solution, the ability to release from eggs, not adults and the multiplier affect which significantly reduces the number of releases, may offer significant improvements here." (P.L. Goodman 0068 p. 2)

Commented [WK10]:
BPPD Response: BPPD will assess the efficacy of the product when the data gathered through this EUP is submitted for a Section 3 commercial registration. Note, N. Rose is affiliated with Oxitec, Ltd.

V. Comments on Trial Parameters

W. Jordan and A. Jones (0327), noting that in a "Federal Register Notice signed on September 5, 2019, the Agency announced the receipt of an application for an Experimental Use Permit (EUP) to evaluate the efficacy of releasing genetically engineered (GE) mosquitoes as a tool for suppression of wild *Aedes aegypti* mosquito populations, stated that:

> " . . . the public should be able to comment on the details of the actual studies proposed." (W. Jordan and A. Jones 0327 p. 1)

Explaining their position, W. Jordan and A. Jones (0327), stated that:

> "In the Notice EPA made a finding, pursuant to 40 CFR 172.11(a), that this proposed EUP is of "regional or national significance" and accordingly invited public comment. However, the announcement provides very little substantive information concerning the details of the release of the GE mosquitoes and, more importantly, how the EUP will be carried out. The only document available for review on Regulations.gov is a letter from the applicant's attorney that describes a very general approach for the proposed Experimental Use Permit. To enable the public to provide meaningful input, the non-confidential portions of the actual EUP application should be available for comment. . . . In absence of information about the design of the efficacy research to be carried out under the EUP, it's difficult for the public to comment in a meaningful way." (W. Jordan and A. Jones 0327 p. 1)

Friends of the Earth (0342) specified that:

> " . . . there is insufficient data . . . , about the sites proposed for release in either Florida or Texas, and about Oxitec's proposed experimental program." (Friends of the Earth 0342 p. 1)

The Center for Food Safety (0344) and GeneWatch UK (0335) called for the following to be supplied to the public:

> "•The GPS coordinates and other relevant details of the proposed release sites and the scientific protocols for the proposed trial
>
> • A proposal for comprehensive post-release monitoring of the proposed releases and their potential impacts on the environment." (Center for Food Safety 0344 p. 18; GeneWatch UK 0335 p. 15-16)

The Center for Food Safety (0344) and GeneWatch UK (0335) also called for the following to be supplied to the public:

> "Information about which existing control methods will continue to be applied during the proposed releases." (Center for Food Safety 0344 p. 18; GeneWatch UK 0335 p. 15-16)

W. Jordan and A. Jones (0327) stated that:

> "Because the proposed EUP concerns the release of GE mosquitoes to suppress wild populations of mosquitoes, and because mosquitoes are a significant public health pest capable of transmitting serious diseases, the EPA should consider this an EUP for a public health pesticide. Accordingly, as with any public health pesticide use, testing done under this proposed EUP should include a detailed, rigorous assessment of the efficacy of the proposed use of GE mosquitoes as a technique for suppression of wild populations." (W. Jordan and A. Jones 0327 p. 1)

Commented [WK11]: BPPD Response: BPPD followed the standard procedure for making information available publicly during the EUP process. The Section G application was throughly screened and reviewed herein by EPA as mosquitos are a significant public health pest. Please see the docket associated with the final decision memorandum which will contain the EUP protocol submitted by Oxitec, Ltd.

W. Jordan and A. Jones (0327) stated that:

> "The EPA science review should include a thorough evaluation of the proposed methods for measuring efficacy under the EUP. If appropriate, EPA should direct the use of multiple methods of obtaining population counts to enhance confidence in the evaluation of efficacy." (W. Jordan and A. Jones 0327 p. 2)

W. Jordan and A. Jones (0327) stated that:

> "If approved, the EUP should be carried out in a manner that clearly isolates the effect of the release of the GE mosquitoes from other nearby mosquito-control efforts such as wide-area adulticide sprays and mosquito larvae control programs or control efforts by private landowners. There should be an assessment of whether the EUP results could have been confounded by other mosquito-control efforts in the same general area." (W. Jordan and A. Jones 0327 p. 2)

W. Jordan and A. Jones (0327) stated that:

> "Mosquito populations naturally fluctuate over time and space due to a variety of factors. To assess the potential impact of environmental factors (e.g., land cover, rainfall, temperature) on wild population levels, the EUP should collect data in a manner that enables comparison of areas into which GE mosquitoes were introduced and similar, geographically proximate areas where there was no such release. The comparison should be a quantitative." (W. Jordan and A. Jones 0327 p. 2)

W. Jordan and A. Jones (0327) stated that:

> "The adequacy of the time-frames for measuring population levels should be specified by the applicant and addressed in the EPA science review." (W. Jordan and A. Jones 0327 p. 2)

W. Jordan and A. Jones (0327) stated that:

> "There should be measurements of the ratio of GE mosquitoes to non-GE mosquitoes in the insects collected to determine population levels." (W. Jordan and A. Jones 0327 p. 2)

W. Jordan and A. Jones (0327) stated that:

> "The prevalence or occurrence of the GE trait over time should be measured to assess how long it takes for the release of GE mosquitoes to affect wild population levels and the durability of the effectiveness of the release of the GE mosquito." (W. Jordan and A. Jones 0327 p. 2)

W. Jordan and A. Jones (0327) stated that:

> "There should be an assessment of the spatial distribution of the trait and whether that changes over time. For example, does the geographic range of the trait change, if at all, beyond the area of the initial release? If yes, how far and how quickly does the trait change spread (or narrow)?" (W. Jordan and A. Jones 0327 p. 2)

W. Jordan and A. Jones (0327) stated that:

> "The EUP should describe the statistical analyses that will be used to assess the data collected." (W. Jordan and A. Jones 0327 p. 2)

Commented [WK12]: I'll clean this up…

BPPD Response: Oxitec has proposed to measure population counts via multiple means – as the adult over-flooding ratio and mating fraction. EPA is in concurrence with the proposed distance between control and treatment sites as long as no OX5034 mosquitos are trapped on the parameter of the dispersal experiments conducted. Studies will continue until no fluorescent OX5034 or offspring mosquitos have been trapped. Trait persistence and spatial distribution measurements will be taken by Oxitec, Ltd.

Anonymous (0023) and Anonymous (0130) stated that:

> "The proposal does not have sufficient information for the public to provide knowledgeable comments. For example, this experiment should have the methodology, planned statistical analysis, adaptive management, etc. for the public to review and comment. Simply stating a brief paragraph about the proposal is not enough information for individuals to analyze the approach of the proposed experiment." (Anonymous 0023 p. 1; Anonymous 0130 p. 1)

Commented [WK13]: BPPD Response: BPPD followed the standard procedure for making information available publicly during the EUP process. The Section G application was throughly screened and reviewed herein by EPA as mosquitos are a significant public health pest. Please see the docket associated with the final decision memorandum which will contain the EUP protocol submitted by Oxitec, Ltd.

GeneWatch UK (0335) stated that:

"According to the summary of the application, the proposed experiments are to evaluate the efficacy of OX5034 mosquitoes as a tool for suppression of wild *Aedes aegypti* mosquito populations. The proposal does not mention any investigations of potential adverse effects on the environment. However, many more such studies (in contained use, and by monitoring and modelling the behaviour of wild mosquito populations and their ecosystems) would be required before an adequate risk assessment could be undertaken." (GeneWatch UK 0335 p. 12)

Commented [WK14]: BPPD Response: Measuring effects on non-target species or environmental concerns is outside the purview of a study targeting efficacy.

Anonymous (0023) and Anonymous (0130) added that:

"Additionally, there is no information regarding why these test areas were selected. It seems odd that Monroe County Florida, a major tourist destination with over 112.8 million tourists each year from around the world (citation: Floridakeystreasures.com) was selected for a test location. This area is limited in space, which means that these test populations will be actively interacting with Florida Keys residents and tourists. There is not enough land to segregate them from the human population. By releasing an unknown experimental mosquito to this area, you are putting millions of people in direct risk and subsequently the entire country, since the majority of these people will travel home. Many tourists drive vehicles down to the Keys and have the potential to trap these mosquitos inside their vehicles, releasing it in an area outside of the test area. Has the Applicant shown sufficient evidence that the mosquitos will remain within the designated test area? It seems unlikely that they will with the amount of human influence in this area. The Applicant needs to select areas with little opportunity for human interaction or demonstrate scientifically that there is 0 risk to the human and natural environment." (Anonymous 0023 p. 1; Anonymous 0130 p. 1)

Anonymous (0209) stated that:

"I totally object to the testing of this pesticide in the Fl. Keys. There are other places that are not inhabited (Everglades, forests, etc.) that are not populated by people where they can test their product. The Fl. Keys are fully inhabited. It makes no sense to test in a highly populated area." (Anonymous 0209 p. 1)

Anonymous (0016) stated that:

"I ask that you diligently deny the permit, ask for much more time and scrutinize with objective fact checkers all their data, and additionally require they find a safe and unpopulated location, or better yet build a biodome to create the most basic of scientific base lines, that being in this case, a potential ground zero." (Anonymous 0016 p. 1)

Commented [WK15]: 1.The Florida Keys are not an appropriate location for the EUP (Anonymous -0023 and -0130)

BPPD Response: The Florida Keys represent a high-risk area for mosquitos and represent a worst-case scenario for pest control. Further, EPA has conducted a human health and environmental risk assessment to address concerns related to off-target risks presented by OX5034.

It is unlikely that *Ae. aegypti* will travel farther than X meters.

R. Marquant III (0235) stated that:

> " . . . in summary of request there was an expectation of up to 6600 acres at 20000 mosquitoes per acre or 132,000,000 mosquitoes per week with no statement on number of weeks the experiment will last nor how Oxitec will deal with unintended results or cross genetic mutations in the public summary. Nor do I see any plan to address issues to public health and economic impact if unexpected results were to occur." (R. Marquant III 0235 p. 1)

Commented [WK16]: BPPD Response: BPPD has conducted a rigorous human health and environmental risk assessment