Friends of the Earth

September 30, 2021

Docket No. EPA-HQ-OPP-2019-0274
OPP Docket
Environmental Protection Agency Docket Center (EPA/DC), (28221T)
1200 Pennsylvania Ave. NW
Washington, DC 20460-0001

Comments for the EPA's consultation on application 93167-EUP-2 from Oxitec

To Mr. Smith and United States Environmental Protection Agency (EPA):

Friends of the Earth (FOE) respectfully submits the following comments on behalf of its over 4 million members and advocates in response to EPA's proposed Experimental Use Permit amendment and extension allowing the release for investigational use of Oxitec, Ltd. (Oxitec)'s genetically engineered (GE) *Aedes aegypti* mosquitoes (OX5034) in California and Florida.

Friends of the Earth is the U.S. voice of the world's largest network of grassroots environmental organizations, with groups in 74 countries. For more than 50 years, Friends of the Earth has worked at the nexus of environmental protection, economic policy and social justice to fundamentally transform the way our country and the world value people and the environment. It is in this light that Friends of the Earth has been following the development of genetic engineering, raising awareness about the environmental and health risks, and the need for more robust government oversight and assessment related to genetically engineered organisms including genetically engineered mosquitoes.

We request that the EPA reject Oxitec's request for an amendment to release OX5034 mosquitoes across 12 undisclosed counties in California and its request for an extension to its Experimental Use Permit (EUP) for the release of genetically engineered mosquitoes in Monroe County, Florida. There should be a full Environmental Impact Statement (EIS) under the National Environmental Policy Act (NEPA) for each of the proposed counties, and this should be reviewed by a committee of independent ecologists and entomologists, public health experts, and other key experts and public stakeholders. There should be long term caged trials in each California county, an endangered species review, and a publicly accessible full CDC review of potential public health impacts. The EPA should release the full data from the current field trials in Monroe County, FL, and Oxitec's full application to the EPA should be publicly available for review. EPA should also convene public meetings in Monroe County, FL and in each of the 12 California counties, advertised in the Federal Register, for the review of the company's proposal and EIS. The EPA should develop new regulations for genetically engineered insects designed to be bio-pesticides -- only after these regulations are in place should EPA consider an application for GE insects.

This docket contains insufficient data and information for a thorough and responsible assessment. While we support the EPA's intentions to limit mosquito populations and the spread of mosquito borne disease, Friends of the Earth believes this experiment with Oxitec's mosquitoes is too risky for Florida and California's ecosystems and public health and is fraught with many unanswered and critical questions.

Background on issue

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Oxitec has applied for an amendment to its permit to do field releases of genetically engineered Aedes aegypti mosquitoes. Oxitec proposes to extend its permit to release GE mosquitoes in Florida for 2 more years, and to expand its experimental releases to 12counties across California.

Oxitec's application proposes that the open release experiments are to evaluate the efficacy of OX5034 mosquitoes as a tool for suppression of wild Aedes aegypti mosquito populations in Florida and California. The application also states that female offspring of the OX5034 mosquitoes in the environment die before they mature into adults, and therefore exposure to biting female mosquitoes is not anticipated. There is incomplete data and testing to substantiate the claim that no females will survive in the environment, particularly given the vast diversity of ecosystems and agricultural systems across California. Both these claims are questioned in the following response.

According to the application amendment, Oxitec proposes to release its GE mosquitoes in Florida for up to 2 more years, across 6,240 acres, and up to 20,000 male GE mosquitoes per acre, per week. It proposes to expand its EUP to release GE mosquitoes across 12 counties in California, across 84,600 acres, and up to 30,000 male GE mosquitoes per acre, per week.

Although Oxitec claims that the GE mosquito could reduce Aedes aegypti mosquito populations, it is uncertain that, even if Aedes aegypti mosquito populations were reduced, there would be a reduction in rates of disease as other mosquitoes also carry dengue, zika, and related viruses. Oxitec has also not provided data to assess whether population reductions of Aedes aegypti, if they did occur, would lead to disease eradication or reduction.

Environmental impacts

Oxitec's application and the publicly accessible information as provided by EPA leaves critical environmental questions to assess. The GE mosquitoes could pose unique risks to the environment in California and Florida, including to endangered species.

It is unclear what the impacts of the GE mosquitoes on wild animals, including endangered or threatened species, and farm animals are. There is no publicly available data about any feeding trials for mammals or birds, which given the prevalence of endangered species in California, is critical. There is also missing information about mosquito predators or prey, which could be impacted by GE mosquito releases and fluctuating mosquito populations. More feeding trials are needed to assess the risk of ingestion to wild species that eat mosquitoes. Ingestion may also be a potential exposure route, as females are expected to die at the larval stage in the water where they breed. There should also be caged trials in each of CA's 12 counties, and in Monroe County, FL, ahead of any open release.

EPA should not assume that all female GE mosquitoes will die, particularly given the prominence of chemicals like tetracycline in the environment in California's vast agricultural areas, which could impact the survival rate of female GE mosquitoes. As noted further below, Oxitec's data about levels of tetracycline in the environment which could trigger survival is redacted, and thus not possible to assess the full risk.

We also need adequate assessment of the potential impacts of increased mosquito populations when the trial GE mosquitoes are initially released in ecosystems, particularly in the12 California counties and the surrounding areas where the mosquitoes could spread. GeneWatch UK's public comments[1] note

that increases in non-target mosquito species as a result of the proposed releases could pose risks to human and animal health, as could increases in the target species in areas neighboring the releases.

The concerns about introgression of the Aedes aegypti into wild type mosquitoes and the potential vectoral capacity have not been addressed, despite evidence from Brazil[2] highlighting that the genetic material from Oxitec's GE mosquitoes were found in wild mosquitoes. The vectoral capacity of Oxitec's GE mosquitoes should be fully assessed, as well as the potential vectoral capacity of hybrid mosquitoes that could carry the genetic material from Oxitec's GE mosquito. This information should be made publicly available ahead of a public comment period.

Oxitec's application does not consider the complexity of ecosystems carefully enough, nor the vast diversity of California's ecosystems across the state. A complete EIS in each county should not only look at the risks from one release, but the potential impacts of releasing millions of mosquitoes on a continual basis and whether the proposed experimental use will cause unreasonable adverse effects on the environment.

Response to tetracycline

Oxitec's GE mosquitoes are engineered to be dependent on the presence of tetracycline and to die in its absence. In theory, the males will mate and then die off while their tetracycline-dependent gene passes onto their offspring. The offspring should die in the late larvae or pupae stage, and *the Aedes aegypti* population in a given area, such as Monroe County and the 12 undisclosed California counties, will theoretically be suppressed.

However, three key factors point to the limits of this hypothesis. First, 3 to 4 percent of Oxitec's mosquitoes survived into adulthood in the lab in the absence of tetracycline despite carrying the lethal gene.[3,4]

Even more concerning, tetracycline is a common antibiotic used in agricultural production. Florida citrus growers use significant amounts of tetracyclines (oxytetracycline) on agricultural lands as a pesticide in efforts to control the bacteria responsible for the Citrus Greening disease. California has massive agricultural regions, and it is necessary to look at levels of tetracycline use in each of the counties targeted for release and to compare this with the levels of tetracycline in the environment that could impact the survival of female GE mosquitoes. EPA has redacted information about tetracycline levels from Oxitec's proposal, however, so it is not possible to assess this potential risk. The significant presence of tetracycline in the environment may obviate the lethal trait in the GE mosquitoes, and their offspring could survive and continue to breed.

Third, tetracycline is also a prevalent compound found in sewage due to contamination from agricultural run-off and consumer disposal. Aedes aegypti may be found to breed in sewage treatment plants, septic tanks, and cesspits in the Florida Keys and in California. [5]

The possible widespread application and presence of tetracycline in the environment could significantly undermine the efficacy of GE mosquitoes to reduce overall mosquito populations. This further accentuates the EPA's need for a complete EIS and more thorough examination of unintended consequences before allowing Oxitec's application to be considered.

Public health concerns

Oxitec's rationale is based on an assumption that mosquito population reduction will reduce or eradicate diseases such dengue and zika. However, Oxitec has not provided the EPA data to support this claim. Even in its trials in Grand Cayman, the company did not demonstrate that reducing overall populations of mosquitoes will reduce or eradicate disease, as dengue is not endemic in the Cayman Islands.[6] Oxitec should provide a specific mechanism through which its proposed releases might reduce the risk of diseases spread through mosquitoes. Without this information, Oxitec's proposed "pesticide" experiment will not address disease reduction.

Oxitec's GE mosquitos could also increase other vectors for diseases like dengue fever. If Oxitec's mosquitoes were to successfully reduce the Aedes aegypti population and reduce competition for breeding sites, there could be a new ecological niche for other pests to fill, such as the Aedes albopictus (Asian Tiger Mosquito). The Asian Tiger Mosquito is one of the most invasive mosquito species, and research has shown it is a possible vector for dengue fever and other tropical diseases, possibly leading to more harm to human health.[7] The Asian Tiger Mosquito is widespread in the USA, including in Florida.[8]

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.

The experimental release of *Aedes aegypti* raises serious concerns about possible negative impacts on public health. Given the high number of mosquitoes that are proposed for release, and based on experience in the Brazil, there is a high likelihood that humans or animals could swallow the GE mosquitoes upon release. As reported in Brazil, because of the high number of GE mosquitoes released, "it's impossible to talk during the liberation sessions without accidentally swallowing a few."[9] The risks of ingestion, whether intentional or unintentional, of GE mosquitoes by mammals, reptiles, birds, or other organisms, have not been adequately assessed.

There are also concerns about the impacts of biting. Oxitec's initial Draft Environmental Assessment (EA) to the Food and Drug Administration (FDA) acknowledges that it is inevitable that some biting female GE mosquitoes will be released. The sorting is conducted by hand and could result in up to 0.5 percent of the released insects being female.[10] If 100 million mosquitoes were released, 0.5 percent could mean that an additional 500,000 biting mosquitoes could be present in the environment.[11] However, checks by the Mosquito Research and Control Unit (MRCU) in the Cayman Islands on one production batch on May 12, 2017 revealed 9 females in one release pot of 500 (1.8%), nine times the agreed level. If the sorting of GE mosquitoes for the field trials were to have similar results as the Cayman Islands, millions of GE female mosquitoes, which can bite and transmit disease, could be released into the environment during the experiments.

Also of concern is that biting female GE mosquitoes may inject a novel engineered protein (*tTAVOX5034 and DsRed2-OX5034)* into humans; Oxitec has yet to conduct or publish any study showing that this novel protein is not expressed in the mosquito's salivary gland, nor has it determined the protein's allergic or toxic potential. Oxitec claims the exposure will be negligible.

However, Oxitec's claim about the potential toxicity or allergenicity from biting GE mosquitos and the lack of exposure to biting females depends on the assumption that females do not survive to adulthood.

In reality, survival may occur if resistance develops or because of environmental exposure to tetracycline (see more detail in the section above and our previous submission[13]).

Lastly, there is concern around the possibility of the dengue virus to evolve and become more potent and virulent in response to the introduction of the GE mosquitoes, and this could put human health at greater risk.[12]

Lack of regulations

No federal agency has formal regulations specific to GE insects and animals. The current U.S. regulatory system is outdated and lacks clear oversight of the use of biotechnology to address insect vectors of animal and human diseases. The EPA should issue new regulations that cover GE mosquitoes before it allows any experimental use of this novel technology.

Regulatory action under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) predominantly focuses on the component which would serve as a pesticide, in this case, the tetracycline Trans-Activator Variant (tTAV) protein that Oxitec's GE mosquitoes have been genetically engineered to express. However, it is critical that the EPA examine the whole mosquito, the method of delivery in this case, and its direct and indirect impacts on the environment, human and animal health.

Also, because the Aedes aegypti mosquito is considered a disease vector, the EPA should clarify the legal basis for a proposal which would allow Oxitec to be released from the contained use requirements of its import permit, as delineated by the Center for Disease Control, in order to allow its GE mosquitoes to be deliberately released into the environment.

Under the National Environmental Policy Act (NEPA), the EPA should consider all environmental effects of the environmental release of Oxitec's GE mosquitoes, analyze potential risks, and analyze alternatives to these actions. As part of these requirements, the EPA should undertake a full EIS so that it may thoroughly examine the potentially substantial impacts that the proposed action may have.

Although, in some cases, proposed actions under FIFRA have been exempt from NEPA, Oxitec's proposed actions for a deliberate release of disease vectors into the environment raise complex environmental issues which may not be adequately captured under FIFRA, therefore an assessment under NEPA should be required.

In addition to preparing a full EIS for public consideration, the EPA should ensure that it is complying with the Endangered Species Act.

Ethical concerns

The release of GE mosquitoes as an attempt to curb the spread of disease should be considered a medical trial and must follow the laws and guidelines in place to protect human subjects in medical trials. Central to ethics on human subject trials is the idea of free and informed consent. However, Oxitec has a track record of releasing GE mosquitoes without public consent, including in their field releases in the Cayman Islands in 2009[13] and in Malaysia in 2010.[14] Throughout the 2021 field trials in Florida, residents consistently asked for the trials to stop, for there to be a process of consent and transparency, and for a process of redress.

EPA notes that consent is not necessary and that this is not a human trial because Oxitec's research "does not meet the regulatory definition of research involving human subjects." This is based on Oxitec's claims that female GE mosquitoes won't survive into adulthood. However, there is not publicly available data to support this company claim. There have not been caged trials in the proposed counties in California that show that females wouldn't survive, particularly in the presence of tetracycline. There is a risk that female GE mosquitoes will survive and could bite people living in the release areas. It is also possible that people in surrounding areas will be affected. Aedes aegypti mosquitoes could move to nearby areas, there could be a hybrid GE-wild type mosquito as was found in Brazil, or other types of mosquitos, like the Aedes albopictus, could move into the open ecological niche and introduce new diseases.

Given these risks, it is critical that all potentially affected communities are given the right to free and prior informed consent to being part of this experiment.

Public transparency

The current information available to the public for review is inadequate and blocks critical information necessary for responsible analysis of environmental and public health risks. In addition, the public engagement process as witnessed in Monroe County, Florida has lacked transparency, been riddled with contradictions, and misled the public.

As with Oxitec's 2018 EUP application for releases in Florida, the lack of transparency and missing information makes any meaningful independent assessment nearly impossible. Information critical for health and environmental analysis is blacked out and withdrawn as Confidential Business Information (CBI). Public health information withdrawn or redacted from the application includes: details about the allergic potential of the fluorescent protein found in the mosquito's saliva, and details about what levels of tetratcycline would allow female GE mosquitoes to survive to adulthood. Given the human populations in California and Florida, this public health information should not be allowed to be withdrawn as CBI. The EPA has also not included the CDC's full advice.

There is also missing information critical for environmental assessments. Neither EPA nor Oxitec publicly name the counties proposed for release. There is no information about populations of Aedes aegypti in California or competitor mosquito species that could move into its ecological niche, and it remains unclear how any analysis about population reduction will be conducted. Despite Oxitec's previous completed field trials in Brazil and Florida, there is still no publicly available data.

In addition to missing public health and environmental data, EPA has not provided potentially affected communities with critical notice about the application. Community members across all 12 counties must be informed of this proposal and amendment, be informed about the public comment period, and have the full information to do assessments related to their communities. However, the counties proposed for release sites in California haven't been formally named, so people will not know if they could be impacted by the proposed release. There should be communication in multiple languages throughout the process of assessment through a number of mechanisms, including the establishment of local institutional review boards and ethics committees and hosting of community meetings and public forums. Community members must know the parameters of the trial areas, have a right to leave the field trial areas, or demand the halt of the experiment entirely if they so decide. [15]

Conclusion

Friends of the Earth believes that there is inadequate information on which to base a public analysis; EPA's docket offers only partial science and analyses. The analyses do not have the necessary data or appropriate risk assessments needed to draw safety conclusions, and the assessments do not adequately address potential unintended consequences. In light of the unanswered questions and the gaps in data analysis, FOE urges EPA to reject Oxitec's amendments and extension requests for genetically engineered mosquitoes to be released in California and Florida. EPA should request further studies from Oxitec and require a full EIS be published for public consultation ahead of an application for an EUP.

Recommendations

Questions remain about the GE mosquitoes' environmental and health impacts as well as their effectiveness in reducing disease. At this point, the EPA should reject Oxitec's application for the release of GE mosquitoes.

The EPA must require Oxitec to obtain the free and informed consent of all potentially affected communities in California and Florida before any trial is allowed to move forward, and mechanisms should be made available to halt the experiment if the community demands. We urge the EPA to conduct a full EIS and to:

- Establish an independent committee of independent ecologists and entomologists, public health experts (including dengue fever and zika virus specialists), and other key experts and public stakeholders to review the proposal and consider the potential environmental, health and social impacts of the release of GE insects;
- Convene public meetings, at various times of the day and evening, across all potentially affected communities for public comment and discussion of the proposal with key independent experts present;
- Develop new regulations for genetically engineered insects that are designed to be bio-pesticides — only after these regulations are in place should EPA, the State of Florida, and the State of California consider an application for the release of genetically engineered insects; and
- Conduct a referendum for Florida and California residents to vote on whether there should be a release of Oxitec's genetically engineered mosquitoes.

Friends of the Earth thanks the EPA for the opportunity to comment on this Pesticide Experimental Use amendment and extension. Until the above requests have been met, the missing information has been provided, and the EPA has formal regulations for the oversight of GE insects, we urge the EPA to not allow any permits for environmental release of genetically engineered mosquitoes to move forward.

Sincerely,

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[1] Public comments from GeneWatch UK. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/genewatch-uk-response-to-the-epa.pdf

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