UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

SUBJECT: Review of the studies submitted detailing the Environmental Exposure to Tetracyclines in Proposed EUP Sites in California for the new end-use product OX5034 *Aedes aegypti* containing tetracycline-repressible transactivator variant protein (tTAV-OX5034, new active ingredient), DsRed2-OX5034 protein (new inert ingredient), and the genetic material necessary (from vector pOX5034) to produce the proteins *in vivo*.

Submission Number:	1067214
Parent Case:	00295568
Action Code Case:	00295569
EPA File Symbol(s):	93167-EUP-2
MRID Numbers:	51361702, 51635004 (Supporting information)

FROM: Nina R. Ortiz, Ph.D., Biologist
Emerging Technologies Branch
Biopesticides and Pollution Prevention Division

NINA ORTIZ Digitally signed by NINA ORTIZ Date: 2021.10.25 16:27:16 -04'00'

THRU: Cassandra Kirk, Ph.D., Biologist
Emerging Technologies Branch
Biopesticides and Pollution Prevention Division

CASSANDRA KIRK Digitally signed by CASSANDRA KIRK Date: 2021.10.25 17:10:39 -04'00'

Wiebke T. Striegel, Ph.D., Senior Scientist
Emerging Technologies Branch
Biopesticides and Pollution Prevention Division

WIEBKE STRIEGEL Digitally signed by WIEBKE STRIEGEL Date: 2021.10.26 09:09:14 -04'00'

Michael Mendelsohn, Branch Chief
Emerging Technologies Branch
Biopesticides and Pollution Prevention Division

MICHAEL MENDELSOHN Digitally signed by MICHAEL MENDELSOHN Date: 2021.10.26 09:17:18 -04'00'

TO: Matthew Weiner, Risk Manager
Emerging Technologies Branch
Biopesticides and Pollution Prevention Division

BACKGROUND:
Oxitec Ltd., (Oxitec or the applicant) submitted information in support of an amendment to their EUP under FIFRA Section 5 for the new end-use product (EP) containing the new active ingredient tetracycline-repressible transactivator variant protein (tTAV-OX5034), the new inert ingredient DsRed2 protein (DsRed2-OX5034), and the genetic material necessary (from vector pOX5034) to produce the proteins *in vivo*. The applicant submitted this amendment for the existing EUP (EPA file symbol 93167-EUP-2) which permits field trials in Harris County, Texas and Monroe County, Florida to assess the ability of the product to suppress local *Aedes aegypti* populations.

Oxitec requested this amendment to 93167-EUP-2 to extend the length of the field trials in Monroe County, Florida by 12 months beyond the current expiration date. The applicant also requested to include multiple field-testing sites for a duration of 24 months in California (up to 12 counties). Under the amended EUP, Oxitec is planning to assess the efficacy and dispersal parameters of the product by testing deployment methods using OX5034 adult male mosquitoes and eggs.

REVIEW:
As part of the risk assessment, EPA evaluates the likelihood for the presence of OX5034 adult female mosquitoes to be present in the environment as those may pose a potential route of exposure through biting. Survival of females into adulthood is conceivable if environmental tetracycline levels in oviposition sites are high enough to rescue the female-specific lethal phenotype. To address this point, Oxitec submitted non-guideline studies (MRID 51361702 and Supporting Information 51635004) in which a literature search was conducted to provide information on previously identified sources of environmental tetracycline and tetracycline analogues (doxycycline, chlortetracycline, and oxytetracycline) at various sites across the United States. In these studies, Oxitec identified wastewater treatment plants, hog lagoons, rivers downstream of agricultural land or swine production facilities, farm springs, and surface water as potential sources and listed out the reported value of tetracyclines found at these sites.

However, that analysis did not identify whether any of these potential sources are present in the proposed California treatment areas nor did it provide information on their location within the treatment areas. This information would be useful to consider when selecting the California Counties and treatment areas in which releases will take place. A map displaying the potential environmental source sites (including but not limited to: citrus groves and other agricultural applications of tetracycline, wastewater treatment facilities, hospital sewage, aquaculture, livestock sewage lagoons; EPA, 2020), the number of these locations within each County, and the methods used to identify these sources should also be included in the analysis.

REFERENCES:
EPA. 2020. Data Evaluation Record – Dose Response of Hemizygous *Aedes aegypti* OX5034 to Tetracyclines and Effects of Environmental Exposure to Tetracyclines. MRID: 50889415