Message

From: Tricia Whitmore [Tricia.Whitmore@oxitec.com]
Sent: 3/3/2017 10:30:22 AM
To: Milewski, Elizabeth [Milewski.Elizabeth@epa.gov]; Wozniak, Chris [wozniak.chris@epa.gov]
CC: Camilla Beech [Camilla.Beech@oxitec.com]; Matthews, Keith [KMatthews@wileyrein.com]
Subject: RE: Oxitec documents for EPA meeting 7 March
Attachments: Response_EPA Questions_tTAV_DsRed2_3 Mar 2017.docx

Hi Elizabeth,

Please find attached Oxitec's responses to your questions.

With best regards,

Tricia

From: Matthews, Keith [mailto:KMatthews@wileyrein.com]
Sent: 01 March 2017 18:47
To: Milewski, Elizabeth <Milewski.Elizabeth@epa.gov>; Tricia Whitmore <Tricia.Whitmore@oxitec.com>; Wozniak, Chris <wozniak.chris@epa.gov>
Cc: Camilla Beech <Camilla.Beech@oxitec.com>
Subject: RE: Oxitec documents for EPA meeting 7 March

Elizabeth,

Thanks for letting us know. I will arrange for the documents to be delivered this afternoon to the address highlighted below. We will do our best to have them delivered by 4:00 p.m., but please let me know if there are time constraints on delivery.

Also, regarding the questions at the end of your message, Oxitec will be developing responses and providing them to you as soon as they can.

Thanks for your patience.

Best,

Keith

Keith A. Matthews | Attorney at Law
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From: Milewski, Elizabeth [mailto:Milewski.Elizabeth@epa.gov]
Sent: Wednesday, March 1, 2017 11:54 AM
To: Tricia Whitmore <Tricia.Whitmore@oxitec.com>; Wozniak, Chris <wozniak.chris@epa.gov>

Cc: Camilla Beech <Camilla.Beech@oxitec.com>; Matthews, Keith <KMatthews@wileyrein.com>
Subject: RE: Oxitec documents for EPA meeting 7 March

Hi, Tricia.

Thanks for the attempt – but our system removed the file. Is there another way you might get the information to us? If there are CBI information in the materials you will be sending, it should be sent through courier service or mail. Obviously for speed, overnight is preferable. If you choose this route:

Via Courier Service Delivery (overnight):
Mike Mendelsohn
Attn: Elizabeth Milewski, Ph.D.
U.S. Environmental Protection Agency
Office of Pesticide Programs (7511P)
Room S8751, One Potomac Yard
2777 Crystal Drive Arlington, VA 22202

Via USPS, please use the following address:
Mike Mendelsohn
Attn: Elizabeth Milewski, Ph.D.
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Office of Pesticide Programs (7511P)
1200 Pennsylvania Avenue, N.W.
Washington DC 20460-0001

As I may have mentioned before – we are most interested at this time in the newest materials on your chart below. – e.g., TES 1, 2, and 3.

Also, we have a few additional questions.

1.) Are there quantitative data on the amounts of tTAV and dsRed proteins in larval or adult mosquitoes?
2.) What is the relative molecular mass for tTAV protein?
3.) How stable is tTAV to changes in ionic strength, pH or other physical conditions (how stable is relative to other proteins)? Is it known to be susceptible to any specific proteases?

Thanks.

From: Tricia Whitmore [mailto:Tricia.Whitmore@oxitec.com]
Sent: Wednesday, March 01, 2017 9:48 AM
To: Milewski, Elizabeth <Milewski.Elizabeth@epa.gov>; Wozniak, Chris <wozniak.chris@epa.gov>
Cc: Camilla Beech <Camilla.Beech@oxitec.com>; Matthews, Keith <KMatthews@wileyrein.com>
Subject: Oxitec documents for EPA meeting 7 March

Hi Elizabeth,

As promised, please find attached pre-reading materials for our meeting on 7 Mar. There are 18 files……. for ease of reference, we have provided a table of contents which lists the files provided.

Table of contents:

Document code	Document title	Results /Conclusion
FTS 1	OX513A *Aedes aegypti*: Suppression Project EastEnd, Grand Cayman, Cayman Islands	96% suppression of local population as measured by the number of mosquito eggs recovered from ovitraps

FTS 2	OX513A *Aedes aegypti*: Suppression Project Itaberaba neighbourhood, Juazeiro (Bahia), Brazil	93% suppression of local population as measured by the number of mosquito eggs recovered from ovitraps
FTS 3	OX513A *Aedes aegypti*: Suppression Project Mandacaru neighbourhood, Juazeiro (Bahia), Brazil	99% suppression of local population as measured by the number of mosquito eggs recovered from ovitraps
FTS 4	OX513A *Aedes aegypti*: Suppression Project Pedra Branca neighbourhood, Jacobina (Bahia), Brazil	92% suppression of local population as measured by the number of mosquito eggs recovered from ovitraps
FTS 5	OX513A *Aedes aegypti*: Suppression Project Nuevo Chorillo, Arraijan, Panama	93% suppression of local population as measured by the number of mosquito eggs recovered from ovitraps
PP1*	Suppression of a field population of Aedes aegypti in Brazil by sustained release of transgenic male mosquitoes Carvalho et al, 2015	Sustained release of OX513A males may be an effective and widely useful method for suppression the key dengue vector Ae. aegypti. The observed level of suppression would likely be sufficient to prevent dengue epidemics in the locality tested and other areas with similar or lower transmission.
PP2*	Short-term suppression of Aedes aegypti using genetic control does not facilitate Aedes albopictus Gorman et al, 2015	There was no evidence for species replacement of Ae.aegypti by Ae.albopictus over the course of this study. No unintentional environmental impacts or elevated operational risks were observed. The potential for this emerging technology to mitigate against disease outbreaks before they become established is discussed.
PP3*	Successful suppression of a field mosquito population by sustained release of engineered male mosquitoes Harris et al, 2012	Validates the potential of OX513A RIDL mosquitoes for population suppression.
PP4	Field performance of engineered male mosquitoes Harris McKerney, 2011	Demonstrated that genetically modified male mosquitoes, released across 10 hectares for a 4-week period, mated successfully with wild females and fertilized their eggs. These findings suggest the feasibility of this technology to control dengue by suppressing field populations of A. aegypti.
PP5	Open Field Release of Genetically Engineered Sterile Male *Aedes aegypti* in Malaysia Lacroix McKerney, 2012	After extensive contained studies and regulatory scrutiny, a field release of engineered mosquitoes was safely and successfully conducted in Malaysia. The engineered strain showed similar field longevity to an unmodified counterpart, though in this setting dispersal was reduced relative to the unmodified strain. These data are encouraging for the future testing and implementation of genetic control strategies and will help guide future field use of this and other engineered strains.
PP6	Mating competitiveness and life-table comparisons between transgenic and Indian wild-type *Aedes aegypti L* Patil et al, 2015	Laboratory study demonstrates that only minor life-table variations of limited biological relevance exist betweenOX513A and Indian Ae.aegypti populations, and males had equal potential formatting competitiveness. Thus, results support the OX513A strain as a suitable candidate for continued evaluation towards sustainable management of Ae. aegypti populations in India.
TES 1	Non-target and threatened and endangered species effects analysis for Monroe County, FL. Prepared FEB 2017 for EPA pre-reading	Proposed trial would not jeopardize the continued existence of any other threatened or endangered species located in Monroe County or result in the destruction or adverse modification of other endangered species' critical habitat due to their being located a considerable distance from the proposed trial site.
TES 2	Threatened and Endangered Species In Monroe County, FL: Lack of Impact From Exposure to OX513A Mosquitoes	Threatened and Endangered Species in Monroe County are not affected by release of OX513A mosquitos.
TES 3	US Dept of the Interior Fish and Wildlife Service: List of threatened and endangered species	There are a total of 43 threatened or endangered species that may occur within boundary of the proposed project. Species on this list should be considered in an effects analysis.
NTO 1 (Study code 232SRFR12C1)	A laboratory prolonged toxicity study to determine the effects of ingestion of larvae and pupae of the genetically modified sterile mosquito strain Aedes aegypti OX513A towards the guppy Poecilia reticulata (Actinopterygii: Poeciliidae); according to OECD No. 204 (1984) modified for oral route of exposure.	There was no significant difference between mortality, fish length, weight, appearance and behaviour in the control and the test item, after 14 days. Hence the NOER was found to be 700 g GM mosquitoes/kg diet and the LOER and LR50/ER50 were estimated to be > 700 g GM mosquitoes/kg diet.
NTO 2	Oral Ingestion of Transgenic RIDL *Ae. Aegypti* larvae has no negative effect on two predator Toxorhynchites Species. Oreenaiza et al, 2011	Results show that Ae. aegypti OX513A RIDL strain is unlikely to have any adverse effects on invertebrate predators in the environment.

FTP	Draft Field Protocol for OX513A	-
* Previously submitted 8 Feb 2017		

I look forward to meeting you both.

With best regards,

Tricia

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