Message

From: Wozniak, Chris [wozniak.chris@epa.gov]
Sent: 2/27/2017 4:52:49 PM
To: Mendelsohn, Mike [Mendelsohn.Mike@epa.gov]
CC: McNally, Robert [Mcnally.Robert@epa.gov]; Hartman, Mark [Hartman.Mark@epa.gov]; Leahy, John [Leahy.John@epa.gov]; Kough, John [Kough.John@epa.gov]; Borges, Shannon [Borges.Shannon@epa.gov]
Subject: RE: Oxitec
Attachments: Problem Formulation-OX513A-022717.docx; Oxitec-EA-Rev-DataNeedsSummary-022617.docx

Flag: Follow up

I am attaching two documents regarding the OX513A product. One is a summary of what Oxitec included in their submission to FDA for the EA last year. The other document is more focused on questions arising from problem formulation / building of a conceptual model relative to release of this male sterile mosquito into the southern US. Hopefully we can discuss these further as meetings on the subject progress through the week.

In digging in to life cycle analysis, I was struck by how the majority of studies I found were examining the 'life cycle' of non-living things (e.g., tires, fan belts, nanomaterials); more concern over environmental fate and recycling than anything else. I've asked Anna for further insight into how she saw LCA fitting into this GE mosquito paradigm and will amend as necessary once I hear from her. My take is that building a conceptual model as part of a problem formulation stage of RA is more pertinent to the task at hand. Given that the OX513A product spends the majority of its life in containment, it is hard for me to see how a life cycle analysis will inform our risk-based questions.

I tried to keep these documents relatively short, but there certainly are other aspects worthy of discussion that may not be included!

Chris

From: Mendelsohn, Mike
Sent: Thursday, February 23, 2017 11:27 AM
To: Wozniak, Chris <wozniak.chris@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Hartman, Mark <Hartman.Mark@epa.gov>; Leahy, John <Leahy.John@epa.gov>
Subject: RE: Oxitec

Chris,

After talking with Mark this morning, we think it would be good if you put together the one pager in time for him to provide feedback on before the meeting next week. We also will need the life-cycle chart. Can you send them to us by 12 pm on Monday to give time for feedback and revision before the 2 pm meeting on Tuesday? Thanks!

Mike

- A life-cycle chart for mosquitoes to work off of to help walk through potential exposures (like Anna described).
- A one pager or chart of sorts describing the pieces of information that FDA considered in their Eco evaluation of Oxytech, and FDA's rationale/conclusions. (Maybe a summary of the FDA assessment?) I think this could help us identify gaps between what they did vs. what we typically do, if there are any.

From: Mendelsohn, Mike
Sent: Wednesday, February 22, 2017 12:16 PM
To: Wozniak, Chris <wozniak.chris@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Hartman, Mark <Hartman.Mark@epa.gov>; Leahy, John <Leahy.John@epa.gov>
Subject: Oxitec

Chris,

It looks like we will be meeting with Oxitec on March 6 or 7th. More to follow. Can you gather folks, particularly John and Shannon, as soon as possible to follow up on the issues below for human health and eco? I would also include Kimberly since she is working with EFED GS-15 biologists to discuss the fate of and non-target exposure to the mosquito products. Thanks!

1) **Discuss what info/data might be required for an Oxitec GE mosquito EUP or Section 18 risk assessment in the context of the EA done by FDA. We need to filter this through an EPA-style/FIFRA risk assessment and what additional data, if any, we need as well as how the data and information should be submitted for us to do our review.**

From: Hartman, Mark
Sent: Thursday, February 16, 2017 2:39 PM
To: Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>; Milewski, Elizabeth <Milewski.Elizabeth@epa.gov>; Tapken, Wiebke <Tapken.Wiebke@epa.gov>; Borges, Shannon <Borges.Shannon@epa.gov>; Wozniak, Chris <wozniak.chris@epa.gov>; Kough, John <Kough.John@epa.gov>; Eiden, Catherine <Eiden.Catherine@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Leahy, John <Leahy.John@epa.gov>
Subject: Eco Assessment for Genetically Modified Mosquitoes

I perused parts of the EA and there appear to be two studies that were conducted with Oxitec mosquitoes on non-target organisms. One was a predatory mosquito that was fed larvae of "modified" and control aegypti and no effects were observed. The second was a guppy feeding study using apparently eggs, larvae and adults which also did not identify a LOEC. Here is the link to the document. http://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM514698.pdf. Summaries of the studies are on pages 87-88.

My basic question are along these lines:

1. If we apply the biochemical data requirements to this case I believe we would ask for avian oral, avian dietary, freshwater fish acute, freshwater invert acute, non-target insect, seedling emergence and veg vigor. No fate unless you move to Tier 2.
    a. I think the plant studies are nor relevant.
    b. Avian seems relevant if birds feed on mosquitoes which they do. How would we devise a feeding study? Would a feeding study using adult mosquitoes be sufficient to cover the acute oral? If not, how would we go about dosing the birds?
    c. Does the guppy study suffice to fulfill the freshwater fish requirement? It is unlikely that it followed our guidelines so are the deviations important/impact the conclusions of the study?
    d. Can aquatic inverts be exposed? If so, how would be suggest dosing for such a study? If not, what is the rationale for making that conclusion?
    e. Does the predatory mosquito study suffice to fulfill the non-target insect requirement? Would this cover dragonflies and other insects that feed on aegypti? Are there insects that feed on adults and, if

so, could the study which used larvae suffice to cover those exposures or would we want a different study? We typically ask for three non-target insect studies for introduction of naturally occurring microbial. Understanding that exposures are different, is it sensible to only ask for one for a GE organism?

f. Is it reasonable to assume that a bee study is not needed based on lack of exposure?
g. Since we know that amphibians feed on mosquitoes would we want a tox study on frogs or would we argue that the exposure would be covered by one of the other studies?

2. Are we comfortable not requiring fate data from the outset especially considering the scrutiny around introducing a novel construct into the environment? Has Oxitec done any work that might be useful to draw conclusions on fate and transport?
3. Would we need estuarine ecotox data given the areas where the mosquitoes would be released?
4. Does the fact that we don't have any mammalian tox data lead to the need for some to cover potential exposure to non-targets? Are we comfortable, if we are able to make the argument of no exposure to humans, registering this with no mammalian tox data? Many times, even when exposure is precluded for some reason, we have a 6-pack. I know this is a human health issue but I snuck it in anyway.
5. My quick read of the EA led me to believe that the eco assessment was largely based on "impacts on populations" as opposed to an EPA-style risk assessment. Are these arguments relevant to our assessment especially in light of the fact that the EA was only covering a very small area of treatment.
6. Are there any changes we would make to any ecotox study we might require given what we know about the construct outputs or are the standard set of parameters sufficient?

2) Per our discussion at the end of today's meeting, I can pull together the EFED GS-15 biologists to discuss the fate of and non-target exposure to the mosquito products (genetic material, Wolbachia microbe, and carrier mosquitoes themselves). In order to facilitate that discussion**, can you guys provide a few things ahead of time:**

- The assessment that RD used to register the pyriproxyfen mosquito dust product. (Is this the trap product? Can I get that assessment ahead of time?)
- A life-cycle chart for mosquitoes to work off of to help walk through potential exposures (like Anna described).
- A one pager or chart of sorts describing the pieces of information that FDA considered in their Eco evaluation of Oxytech, and FDA's rationale/conclusions. (Maybe a summary of the FDA assessment?) I think this could help us identify gaps between what they did vs. what we typically do, if there are any.

I think we can probably talk about ESA & getting to a no-effect finding in more detail at the same time.

Thanks,
Kimberly

Mike Mendelsohn, Acting Chief
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division (7511P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington DC 20460
(703) 308-8715
(703) 463-7302 Mobile