Message

From: McNally, Robert [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=EFA5514317E34B9895687D73730FDDE9-ROBERT MCNALLY]
Sent: 10/7/2019 4:21:26 PM
To: Mendelsohn, Mike [mendelsohn.mike@epa.gov]
CC: Overstreet, Anne [overstreet.anne@epa.gov]
Subject: FW: 2nd Gen Oxitec (OX5034) EUP Application

Let's chat about this.

From: Keigwin, Richard <Keigwin.Richard@epa.gov>
Sent: Friday, October 04, 2019 4:33 PM
To: Miller, Wynne <Miller.Wynne@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>; Overstreet, Anne <overstreet.anne@epa.gov>; Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>
Subject: RE: 2nd Gen Oxitec (OX5034) EUP Application

Thanks Wynne.

I think part of the request for December accounts for review times in the states. Have we been able to explore co-review by key states (e.g., Florida comes to mind).

From: Miller, Wynne <Miller.Wynne@epa.gov>
Sent: Friday, October 04, 2019 4:31 PM
To: Keigwin, Richard <Keigwin.Richard@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>; Overstreet, Anne <overstreet.anne@epa.gov>; Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>
Subject: Re: 2nd Gen Oxitec (OX5034) EUP Application

Bob,
Alex indicated December if possible since CDC and the company are concerned about having something in time for mosquito season. Maybe see if we can incorporate having CDC a dress the introgression issue for us. Alex mentioned that they are coming in on Oct 16 and maybe that we ask them to help on this aspect. We did tell her that we are concerned about resources since it's the same team working on GE pips. She recognized but said we need to figure out how to make the schedule work for this. Even if not December - shortly thereafter. So please draft a new schedule.
Thx
Wynne

Sent from my iPhone

On Oct 4, 2019, at 4:04 PM, Keigwin, Richard <Keigwin.Richard@epa.gov> wrote:

> Thanks Bob. Regarding the schedule, I think there was some discussion about this during this week's OPP General. I defer to Ed/Wynne, since I wasn't there.
>
> ---
>
> **From:** McNally, Robert <Mcnally.Robert@epa.gov>
> **Sent:** Friday, October 04, 2019 1:37 PM
> **To:** Keigwin, Richard <Keigwin.Richard@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>; Miller, Wynne <Miller.Wynne@epa.gov>
> **Cc:** Overstreet, Anne <overstreet.anne@epa.gov>; Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>
> **Subject:** 2nd Gen Oxitec (OX5034) EUP Application

Rick,

We will construct a schedule that has us reaching an Oxitec decision in mid-December – is that what you want to see?

If not mid-December, what date?

At this point, we are planning to send Oxitec a 75 day letter to get more information on the introgression issue and perhaps other issues. We have had preliminary conversations with them alerting them to this. To theoretically make a mid-December date, we would need to have Oxitec get us the data/information very quickly. If Oxitec took the full 75 days, we would be right at the mid-December date the company told Alex they would need a favorable decision to be able to release mosquitoes this spring.

We will likely have a lot of comments to review, respond to, and factor into the risk assessment. The comment period closes a week from today. As of earlier in the week, we had less than 100 comments. I would suggest we have OGC review our response to comments document. As you may recall from last FY, we received over 250,000 comments on the previous Oxitec application and it was taking 6 months or more to work through them, draft responses and get OGC concurrence. IF some of the comments are the same, the previous effort may help us. Of course, this time, we have the new issue of introgression.

On the introgression issue, we believe the issue is legitimate as outlined in the Nature paper. The other editorializing and commentary in the discussion section, is not supportable.

So, even if the paper is withdrawn, much like the allergenicity issue with the Akane paper, we believe the Brazilian data supports the notion that introgression occurs. In fact, Oxitec's earlier outreach on the new application highlighted the benefits of introgression in overcoming insecticide resistance in native populations.

We have reached out to CDC this week and had a preliminary conversation. We plan to have more next week, and follow-up discussions with Oxitec.

We will keep you posted.

Bob

From: Keigwin, Richard <Keigwin.Richard@epa.gov>
Sent: Monday, September 30, 2019 8:15 PM
To: Miller, Wynne <Miller.Wynne@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Overstreet, Anne <overstreet.anne@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Subject: Re: 2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper 1 Pager and Updated Schedule

I like the idea of reaching out to CDC and FDA now.

Unfortunately, I think both schedules are pretty firm. I think the Oxitec review requires a rather exquisite skill set. I appreciate that the GE rule also requires us to consider some significant science

issues, but perhaps not to the same degree. What skill sets might exist in other parts of BPPD and/or the program to help out?

We will likely have to present Alex with some options for trade-offs other than these two actions.

Rick Keigwin
Director, Office of Pesticide Programs
U.S. Environmental Protection Agency
Phone: 703-305-7090
Website: www.epa.gov/pesticides
Sent from my iPhone

On Oct 1, 2019, at 12:57 AM, Miller, Wynne <Miller.Wynne@epa.gov> wrote:

> If CDC wants this done, then let's have them help? How about if we ask CDC and FDA for input on the introgression issue now (and not wait for the peer review)? Maybe a formal request letter to them … asking for formal response … just a thought.
>
> ---
>
> **From:** McNally, Robert <Mcnally.Robert@epa.gov>
> **Sent:** Monday, September 30, 2019 7:38 PM
> **To:** Miller, Wynne <Miller.Wynne@epa.gov>; Overstreet, Anne <overstreet.anne@epa.gov>
> **Cc:** Keigwin, Richard <Keigwin.Richard@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
> **Subject:** RE: 2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper 1 Pager and Updated Schedule
>
> It might be good if we could discuss this with her.
>
> We are supportive of getting this done as soon as we can, in a way that honors the public comment process, has scientific integrity, and will not result in legal vulnerabilities subsequently. We think this technology has a lot of benefits. However, not doing due diligence will only set back these important new tools. I would think the company and CDC would be concerned about that, as would the Administrator, if I understand his significant concerns with GMO and genetic engineering.
>
> In particular, in my judgment, EPA does not possess the expertise on its own to adequately assess the disease transmission piece highlighted in the Nature article. CDC and FDA, as I understand it, have the skill set given their mandates. Hence, our recommendation for a peer review, which takes additional time.
>
> We also want to deliver her the GE rule on time using the essentially the same staff – some of our best and brightest. I am confident we can get the GE rule to Alex by around Thanksgiving – I am treating that as our #1 priority.
>
> We are open to your suggestions on how we can wrap up Oxitec and the GE rule by December.
>
> Thanks
>
> Bob

From: Miller, Wynne <Miller.Wynne@epa.gov>
Sent: Monday, September 30, 2019 7:16 PM
To: McNally, Robert <Mcnally.Robert@epa.gov>; Overstreet, Anne <overstreet.anne@epa.gov>
Cc: Keigwin, Richard <Keigwin.Richard@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Subject: FW: 2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper 1 Pager and Updated Schedule

Bob – see Alex's comment.

From: Dunn, Alexandra <dunn.alexandra@epa.gov>
Sent: Monday, September 30, 2019 6:43 PM
To: Miller, Wynne <Miller.Wynne@epa.gov>; Siciliano, CarolAnn <Siciliano.CarolAnn@epa.gov>
Cc: Messina, Edward <Messina.Edward@epa.gov>; Keigwin, Richard <Keigwin.Richard@epa.gov>
Subject: RE: 2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper 1 Pager and Updated Schedule

The company and CDC indicated they needed to move forward this year. Please clarify.

Alexandra Dapolito Dunn, Esq.
Assistant Administrator
Office of Chemical Safety and Pollution Prevention
U.S. Environmental Protection Agency
(202) 564-2910
dunn.alexandra@epa.gov

From: Miller, Wynne <Miller.Wynne@epa.gov>
Sent: Monday, September 30, 2019 11:07 AM
To: Dunn, Alexandra <dunn.alexandra@epa.gov>; Siciliano, CarolAnn <Siciliano.CarolAnn@epa.gov>
Cc: Messina, Edward <Messina.Edward@epa.gov>; Keigwin, Richard <Keigwin.Richard@epa.gov>
Subject: FW: 2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper 1 Pager and Updated Schedule
Importance: High

Alex .. FYI ... here's the schedule for Oxitec.
Wynne

From: McNally, Robert <Mcnally.Robert@epa.gov>
Sent: Monday, September 30, 2019 10:26 AM
To: Messina, Edward <Messina.Edward@epa.gov>; Miller, Wynne <Miller.Wynne@epa.gov>
Cc: Overstreet, Anne <overstreet.anne@epa.gov>; Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>
Subject: 2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper 1 Pager and Updated Schedule
Importance: High

Here you go.

We feel some type of peer review is critical, particularly on the issue of potential disease transmissibility, since that is not OPP's area of expertise compared to CDC or FDA. We have provided two options for a peer review – internal gov't and external gov't.

Bob

From: Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>
Sent: Monday, September 30, 2019 10:20 AM
To: McNally, Robert <Mcnally.Robert@epa.gov>; Overstreet, Anne <overstreet.anne@epa.gov>
Cc: Bohnenblust, Eric <Bohnenblust.Eric@epa.gov>
Subject: 2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper 1 Pager and Updated Schedule

Attached are the 1 pager and updated schedule for Oxitec in light of the recent Nature paper.

2nd Gen Oxitec (OX5034) EUP Application and September 2019 Nature Research Paper

Issue: Evans *et al.*, 2019 paper in Nature Research[1] contradicts Oxitec's hypothesis that mosquito lab strain genes will disappear quickly from the environment. The data and methods appear to be scientifically sound and increases OPP concern regarding the introduction of mosquito lab strain genes into natural mosquito populations for the pending Oxitec EUP application.

Action in Review

- OCSPP is currently reviewing an application Oxitec submitted for an Experimental Use Permit (EUP) to test the efficacy their 2nd Generation OX5034 mosquitoes. If approved by EPA, Oxitec would conduct experimental trials in Florida and Texas next year.

Action Timeline

- *March 11, 2019*: Oxitec submitted application for an EUP.
- *July 1, 2019*: EPA sent 10-day deficiency letter noting critical deficiencies in the application.
- *July 16, 2019*: Oxitec submitted response to 10-day deficiency letter.
- *August 26, 2019:* Oxitec submitted additional critical data supplementing existing submissions; EPA had not determined whether the response to the 10-day letter was sufficient to pass the 90-day screen.
- *September 10, 2019:* Evans *et al.*, *Nature Research* paper publishes.
- *September 11, 2019:* Notice of Receipt published beginning a 30-day public comment period. Oxitec originally requested that EPA not publish NOR until after EPA confirmed the application passed the 90-day screen. Around August 26, Oxitec requested EPA no longer wait to confirm the application passed the 90-day screen prior to publishing the NOR. The NOR was working through typesetting for FR publication at this time and OCSPP decided to confirm the application passed the 90-day screen prior to publishing the NOR.

[1] https://www.nature.com/articles/s41598-019-49660-6

- *October 11, 2019*: Comment period closes.
- *November 1, 2019*: Current PRIA date – will need to be renegotiated to allow time to address comments, complete risk assessments, have peer review of assessments, OGC and management review of decision.
- *June 2020*: Estimate of new PRIA date needed with internal government HHS/CDC peer review.
- *January 2021*: Estimate of new PRIA date needed with external SAP.

Synopsis of Public Comment through Sept. 27, 2019

- EPA has received 58 public comments so far. Four (4) commenters have requested an extension of the comment period.
- 21 of which reference the recent Evans *et al.*, 2019 publication or information from news articles about the paper including three comments requesting an extension of the comment period to assess the results in the Evans *et al.*, 2019 publication in relation to the current application.
    - Several of these comments mention the need to assess and minimize risk of gene movement and have mitigation strategies in place in the event introgression occur if this application is approved.
    - Several commenters referencing the article, who indicate they are otherwise supportive of GM technology, are opposed to OX5034 mosquito releases unless risks associated with introgression (e.g., potential for increased disease transmission) can be addressed. They do not want to let the "genie out of the bottle."
- Other issues mentioned are antibiotic resistance, risk to non-target organisms, informed consent.
- EPA anticipates numerous additional comments prior to October 11, some notable NGOs such as the Center for Food Safety from whom we typically receive comment have not provided comment at this time.

Background

- Oxitec withdrew their prior applications for an EUP and registration for OX513A, the 1st generation product to EPA. Their application for OX513A was approved in Brazil and mosquitoes were subsequently released.
- OCSPP has completed the initial screening level review of Oxitec's OX5034 and has moved the application into full review.
- 2nd Gen Oxitec mosquitoes (OX5034) allow for male survival and subsequent reproduction in the environment and thus the likely introduction of lab strain genes into the wild mosquito population (i.e., introgression).
- OCSPP identified the possible movement of genes from the released OX5034 mosquitoes into the wild mosquito populations as a potential issue in pre-submission meetings and again after submission of the application.
- Evans *et al.*, 2019 (published Sept 10) contradicts Oxitec's hypothesis that lab genes will disappear quickly from the environment. The article examines Oxitec's 1st generation GE mosquito where this is less of a risk. Yet, it demonstrates the movement of genes is occuring.
- This issue is credible and deserves scientific scrutiny since the current EUP application before OCSPP (2nd generation OX5034) is expected to have a greater risk of gene movement into the wild mosquito population. While the data in the Evans *et. al.* paper is sound, we recognize that many of the points in the discussion section are not supported by the actual data in the paper.
- OPP does not know at this point whether the Oxitec's 2nd generation OX5034 lab strain has genes that would increase the likelihood of disease transmission.

However, increased disease transmission could be possible and movement of the lab strain genes into the environment in Florida or Texas could be permanent and not limited to the experimental use permit.

- We note that Oxitec has filed a complaint to Nature Research concerning what they consider misleading and speculative statements, https://www.oxitec.com/news/oxitec-response-scientific-reports-article

Potential next steps

Ex. 5 Deliberative Process (DP)