

RECORD OF TELEPHONE CONVERSATION

Submission Information

Application Type	BLA
STN	125428/0.
Review Office	OVRR
Applicant	Dynavax Technologies Corporation / Lic. # 1883
Product	Hepatitis B Vaccine (Recombinant), Adjuvanted
Trans-BLA Group:	No

Telecon Details

Telecon Date/Time	26-APR-2016 1:52 PM
Author	BERKHOUSEN, KATHERINE
EDR	No
Post to Web	No
Outside Phone Number	
FDA Originated?	Yes
Communication Categories	AD - Advice
Related STNs	None
Related PMCs	None
Telecon Summary	CBER response to Dynavax questions Maj Amendment
FDA Participants	Katherine Berkhausen; Richard Daemer
Applicant Participants	Elaine Alambra

Telecon Body:

From: Berkhausen, Katherine

Sent: Tuesday, April 26, 2016 1:52 PM

To: 'Elaine Alambra'

Cc: Daemer, Richard J.

Subject: RE: HEPLISAV BLA 125428 - Follow up on Telecom Request

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Dear Elaine,

We are providing responses in *bold font* to Dynavax' s questions outlined in Dynavax' s email (below) dated April 21, 2016.

Given the notification of the increased review time of the HEPLISAV BLA, Dynavax would like to discuss the following:

1. Can the Agency share the reason(s) for the request for the HBV-10 and 16 datasets at this time? Are there any questions about the datasets that Dynavax can answer at this point in the review?

We review the totality of the relevant clinical data in our assessment of products for licensure. Further, you have submitted revised clinical study reports for these two pivotal studies. We are interested in the extent and nature of revisions to these datasets in order to determine if any conclusions about the product may be affected.

2. We would appreciate understanding the Agency's determination that the April 8th submission contained a substantial amount of new data and thus was a major amendment. **Please see our response to question 1.** We ask because the Agency agreed in the pre BLA meeting in 2011 for Dynavax to provide only the datasets for the integrated analyses, and during the initial review in October 2012 the HBV-16 datasets were provided to the Agency (SEQ 0011) in response to an information request. The datasets provided in April 2016 in response to the Agency's request are those related to the *revised* CSRs. If helpful, Dynavax can itemize which datasets have been revised as a result of the *revised* CSRs.

We will provide an information request describing what information should be submitted.

3. When might the Agency notify Dynavax about **GCP inspection** dates and when might they occur? Does the Agency anticipate conducting a Sponsor site inspection?

FDA will notify the site point of contact for any potential inspection prior to the actual inspection. Any potential sponsor site inspection would be communicated to Dynavax in a timely manner.

- a. Has the Agency determined whether there will be a **VRBPAC** for HEPLISAV? If there will be one, when is it likely to occur? We ask for planning purposes, as preparation will require a significant outlay of time and resources by Dynavax and planning would need to begin soon.

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At this time, we anticipate that discussion of the clinical safety data may take place at a November VRBPAC. We will inform you as soon as possible when a final determination is made.

- b. If there will be a VRBPAC, are there any issues Dynavax needs to address either now or in the Briefing Book?

We will inform you prior to any VRBPAC to ensure that you have adequate preparation time.

- 4. Is the **mid-cycle review** for the HEPLISAV BLA still scheduled for Day 74 from the filing date – in the case of our BLA, that would be 28th of May?

Please note that complete response resubmissions are not subject to the midpoint meeting components under “The Program” of PDUFA V. The review team will meet regularly to target completion of the review by the action due date.

- 5. Can the Agency share any thoughts on their assessment of the “Takayasu’s arteritis” case and can Dynavax respond to any concerns now?

Your application is under active review. We do not have any requests for Dynavax in this regard at this time.

- 6. We would appreciate any feedback the Agency can provide in terms of the BLA and how the BLA review is going at this point.

Your application is under active review. You can expect an Information Request in the next week.

- 7. We would like to do everything we can to assist the Agency as it conducts its BLA review. What can Dynavax can do to help facilitate the review? Would the Agency be amenable to periodic status discussions with Dynavax?

We will contact you if we require further information.

Kind regards,
Katherine Berkhausen

From: Elaine Alambra [<mailto:EAlambra@dynavax.com>]
Sent: Thursday, April 21, 2016 10:16 PM
To: Berkhausen, Katherine

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Cc: Daemer, Richard J.

Subject: RE: HEPLISAV BLA 125428 - Follow up on Telecom Request

Dear Katherine,

Given the notification of the increased review time of the HEPLISAV BLA, Dynavax would like to discuss the following:

1. Can the Agency share the reason(s) for the request for the HBV-10 and 16 datasets at this time? Are there any questions about the datasets that Dynavax can answer at this point in the review?
2. We would appreciate understanding the Agency's determination that the April 8th submission contained a substantial amount of new data and thus was a major amendment. We ask because the Agency agreed in the pre BLA meeting in 2011 for Dynavax to provide only the datasets for the integrated analyses, and during the initial review in October 2012 the HBV-16 datasets were provided to the Agency (SEQ 0011) in response to an information request. The datasets provided in April 2016 in response to the Agency's request are those related to the *revised* CSRs. If helpful, Dynavax can itemize which datasets have been revised as a result of the *revised* CSRs.
3. When might the Agency notify Dynavax about **GCP inspection** dates and when might they occur? Does the Agency anticipate conducting a Sponsor site inspection?
 - a. Has the Agency determined whether there will be a **VRBPAC** for HEPLISAV? If there will be one, when is it likely to occur? We ask for planning purposes, as preparation will require a significant outlay of time and resources by Dynavax and planning would need to begin soon.
 - b. If there will be a VRBPAC, are there any issues Dynavax needs to address either now or in the Briefing Book?
4. Is the **mid-cycle review** for the HEPLISAV BLA still scheduled for Day 74 from the filing date – in the case of our BLA, that would be 28th of May?
5. Can the Agency share any thoughts on their assessment of the "Takayasu's arteritis" case and can Dynavax respond to any concerns now?
6. We would appreciate any feedback the Agency can provide in terms of the BLA and how the BLA review is going at this point.
7. We would like to do everything we can to assist the Agency as it conducts its BLA review. What can Dynavax do to help facilitate the review? Would the Agency be amenable to periodic status discussions with Dynavax?

Thank you for shepherding this through.

Kind regards,

Elaine

Elaine Alambra • Senior Director, Regulatory Affairs • Dynavax Technologies Corporation ☎ Tel: 510-665-0474 ✉ email: ealambra@dynavax.com