

RECORD OF EMAIL CONVERSATION

Submission Information

Application Type	BLA
STN	125428/0.0
Review Office	OVRR
Applicant	Dynavax Technologies Corporation / Lic. # 1883
Product	Hepatitis B Vaccine (Recombinant), Adjuvanted
Trans-BLA Group:	No

Telecon Details

Telecon Date/Time	10-JAN-2017 12:57 PM
Author	BERKHOUSEN, KATHERINE
EDR	No
Post to Web	No
Outside Phone Number	
FDA Originated?	No
Communication Categories	MCA - Meeting Communications - Additional
Related STNs	None
Related PMCs	None
Telecon Summary	Dynavax communicating which questions to discuss at Type A Meeting after having received CBERs written responses to their questions.
FDA Participants	Katherine Berkhausen
Applicant Participants	Elaine Alambra

Email Body: In preparation of the Type A Meeting later this day, Dynavax has provided feedback to CBERs written responses to the Type A Meeting Request/briefing packet questions; which were conveyed via FAX on January 9, 2017. Dynavax proposes to only discuss specific questions where they require more clarification and has outlined those in the email below as well as providing additional clarification of Question 3a.

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Sent: Tuesday, January 10, 2017 12:57 AM

To: Berkhausen, Katherine

Cc: Daemer, Richard J.

Subject: HEPLISAV BLA 125428 / Further Clarification for 10 Jan 2017 Telecom

Dear Katherine,

Dynavax acknowledges and thanks the Agency for their response (received 09 Jan 2017) to the clarification questions we posed in our Type A meeting request (submitted 13 Dec 2016). We look forward to our telecom tomorrow morning.

In preparation of our telecom and to facilitate our discussion, Dynavax is providing the following:

- Dynavax participants

Elaine Alambra	Senior Director, Regulatory Affairs
Mike Berry, PhD	VP, Process Development and Manufacturing Sciences
Graeme Currie, PhD	VP, Clinical Science and Operations
Martin Gohlke, PhD	Senior Director, Analytical Technologies
Randall Hyer, MD, PhD	VP, Medical Affairs
Robert Janssen, MD	CMO and VP, Clinical Dev & Regulatory Affairs
David Novack	Senior VP, Technical Operations

- Comments on the Agency's response

Question 1(a):

1(a)i No further questions

1(a)ii No further questions

1(a)iii Request further discussion

Question 1(b): Request further discussion

Does the Agency have criterion for the minimum size of an imbalance?

Question 2: No further questions

Question 2(a): Request further discussion

Question 2(b): No further questions

Question 2(c): No further questions

Question 2(d): No further questions

Question 2(e): No further questions

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Question 3(a):

- 3(a)i Further clarification provided (see below); Request further discussion
- 3(a)ii Request further discussion
- 3(a)iii Request further discussion

Question 3(b): Request further discussion

Clarification for Question 3(a)i:

The agency asked for clarification regarding which impurities are included in the calculation of the (b) (4) result, namely (b) (4). The agency also stated that that (b) (4)

Dynavax would like to clarify the (b) (4) of the respective impurities and what impurity may contribute to the (b) (4) value for 1018.

Dynavax indicated in the briefing package that a minor impurity, (b) (4), can (b) (4) with the main compound. The (b) (4) impurity is a (b) (4) is controlled by (b) (4) and is measured as one of the unspecified impurities in 1018 drug substance. The acceptance criterion is not more than (b) (4) not a *degradation* product and as such, cannot increase with storage of 1018 or HEPLISAV.

The (b) (4) impurity has a different structure than the (b) (4) impurity, which (b) (4) earlier than the main compound. (b) (4) is a (b) (4). A (b) (4) indicating the (b) (4) impurities and main compound (Figure 4 from the validation report VAL-Q234B-R) is provided below. The (b) (4) impurity (b) (4) with (b) (4) and is therefore not indicated on this (b) (4).

Figure 4. (b) (4) of 1018

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(b) (4)

1018 (b) (4) is calculated as (b) (4). As the (b) (4) impurity (b) (4) with main compound, the 1018 integrity value may include a small contribution from this impurity, but can never be (b) (4) considering the controls at the drug substance stage, as described above.

Kind regards,

Elaine

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