

# RECORD OF TELEPHONE CONVERSATION

## Submission Information

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

## Telecon Details

|                                 |   |
|---------------------------------|---|
| <b>Telecon Date/Time</b>        | 16-SEP-2016 02:32 PM  |
| <b>Author</b>                   | ZUBKOVA, IRYNA  |
| <b>EDR</b>                      | No  |
| <b>Post to Web</b>              | No  |
| <b>Outside Phone Number</b>     |   |
| <b>FDA Originated?</b>          | Yes   |
| <b>Communication Categories</b> | AD - Advice<br>IR - Information Request   |
| <b>Related STNs</b>             | None  |
| <b>Related PMCs</b>             | None  |
| <b>Telecon Summary</b>          | CMC IR for revised process control strategies; revised stability protocols; advised not to use new working cell banks without prior review and approval by CBER |
| <b>FDA Participants</b>         | Katherine Berkhausen; Richard Daemer  |
| <b>Applicant Participants</b>   | Elaine Alambra  |

**Telecon Body:** Email to Dynavax as per below:

**From:** Berkhausen, Katherine

**Sent:** Friday, September 16, 2016 2:32 PM

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**To:** Alambra, Elaine  
**Cc:** Berkhausen, Katherine; Daemer, Richard J.  
**Subject:** IR CMC related

Dear Elaine,

We have the following comments and requests regarding CMC for STN 125428:

1. We note that in Section 3.2.S.2.3.3.6 (New Working Cell Banks) you propose to manufacture, test, and release new working cell banks according to the protocol "Manufacturing and Testing of Working Cell Banks". Requests to use new working cell banks and/or a comparability protocol for qualification of new working cell banks should be submitted as supplement(s) post licensure. Please be advised that any supplement certifying a new working cell bank for use in the manufacturing process should include test results for the new working cell bank qualification and results of analytical tests performed on the first drug substance lot manufactured with the new working cell bank. Please confirm that no new working cell banks will be qualified and introduced into the manufacturing process without prior review and approval by CBER.
2. Regarding the proposed shelf life of the two drug substances and the final drug product. At this time, we will allow a shelf life for the HBsAg drug substance of no longer than (b) (4), a shelf life for the 1018 adjuvant drug substance of no longer than (b) (4) (when stored in (b) (4) containers) and a Heplisav drug product shelf life of no longer than 36 months. We are (b) (4) your proposed shelf life due to insufficient data in support of a 36 month shelf-life for Drug Product manufactured from (b) (4) old HBsAg and (b) (4) old 1018 adjuvant produced at commercial scale. In addition, we are concerned about the loss of (b) (4) during accelerated stability studies of the (b) (4). Please note that the proposed shelf life for the 1018 adjuvant does not include 1018 stored in (b) (4) containers as the available data is limited and show that the (b) (4) is out-of-specification beginning at (b) (4) (b) (4). Until sufficient and satisfactory data is obtained, 1018 adjuvant stored in (b) (4) containers cannot be used for formulation of Heplisav drug product. Please acknowledge this communication and submit new stability protocols that incorporate these designated time periods.
3. In your response to CBER's Information Request of July 7, 2016 you requested several changes to in-process and release testing for the HBsAg bulk. Below are the CBER responses to these requests.
  - a) Response to request in question #5

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Regarding your request to exclude (b) (4) testing from routine in-process testing, at this time we do not agree with the removal this test from in-process testing during HBsAg Bulk manufacturing. Please submit a revised process control strategy for Sections 3.2.S.2.4 and 3.2.S.2.5 that include the following in-process tests:

(b) (4)

b) Response to request in question #6

Regarding your proposal to perform testing of (b) (4) only as an in-process test and exclude it from the release testing. At this time we do not agree with this proposal. Please submit a revised list of release tests for HBsAg Bulk that includes testing for (b) (4) together with the release specification.

Please submit your responses to this request by Sep 26, 2016.

Kind regards,

*Katherine*

Katherine Berkhausen  
CAPT., US Public Health Service

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