

RECORD OF TELEPHONE CONVERSATION

Submission Information

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| 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

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| Telecon Date/Time | 07-JUL-2016 02:08 PM |
| Author | BALDWIN, BRENDA; ZUBKOVA, IRYNA; MAJOR, MARIAN |
| EDR | Yes |
| Post to Web | No |
| Outside Phone Number | |
| FDA Originated? | Yes |
| Communication Categories | IR - Information Request |
| Related STNs | None |
| Related PMCs | None |
| Telecon Summary | CMC items |
| FDA Participants | Katherine Berkhausen |
| Applicant Participants | Elaine Alambra |

Telecon Body:

From: Berkhausen, Katherine
Sent: Thursday, July 07, 2016 2:08 PM
To: Alambra, Elaine

RECORD OF TELEPHONE CONVERSATION

Cc: Daemer, Richard J.

Subject: 125428/0 Information Request - CMC

Dear Elaine,

We continue to review your submission BL 125428/0 and have the following information request.

1. During review of Heplisav stability data, we note that several time points for potency assay results were invalid or invalidated (Lots (b) (4)). Please provide the original potency results for these batches and justify the invalidation of these results.
2. You propose a shelf-life of 36 months for the Heplisav Drug Product stored at $5^{\circ}\text{C}\pm 3^{\circ}\text{C}$. Please provide 36 months stability data for the Heplisav Drug Product lots formulated with HBsAg bulk held for the proposed bulk shelf life of (b) (4) and with the 1018 ISS drug substance held in the (b) (4). These lots should be manufactured using the proposed commercial scale using the validated manufacturing process.
3. We note that within your current submission under Section 1.11.1 “Information Request 10 – Dynavax Proposes” on page 4 of 6 you request “2. Removal of Sterility Test as a Release Parameter for HBsAg (b) (4)”. However, the text discusses the removal of the sterility test during stability studies, not at release. Please clarify if this request is to remove sterility testing for the (b) (4) at release or during stability testing.
4. In Section 1.11.1 “Information Request 10 – Dynavax Proposes”, you propose to remove (b) (4) as a release test for HBsAg bulk. We do not agree with the removal of this test. Please include this test with acceptance criteria and submit a revised list of release tests for the HBsAg bulk and also submit a revised Lot Release Protocol that includes this test.
5. In your response to CRL Question 4, FDA 483 Observation 3.a-f you proposed to remove in-process tests for (b) (4) during manufacture of the HBsAg bulk. At this time we do not agree with the removal of these in-process tests during HBsAg bulk manufacture. As stated in a previous communication from CBER on February 9, 2016, you should submit data to support these changes as a post approval supplement following licensure, at which time the changes will be reviewed. Please submit revised process control strategies for Sections 3.2.S.2.4 and 3.2.S.2.5 that include these in-process tests with acceptance limits.

RECORD OF TELEPHONE CONVERSATION

6. In your response to CRL #41, you propose that (b) (4) be excluded from commercial HBsAg drug substance release testing. We do not agree with the proposal. Please submit a revised list of release tests for HBsAg bulk that includes testing of (b) (4) together with release specifications.
7. In response to a CBER request in 2012 to include (b) (4) as a commercial release test for the HBsAg bulk, Dynavax acknowledged this request and committed to include a test for (b) (4) in the HBsAg Drug Substance release specification (September 26, 2012). This test is not included as a release specification. Please include this test and submit a revised list of release tests for HBsAg bulk.
8. The rationale for not establishing a (b) (4) for the 1018 and instead proposing a (b) (4) is acceptable. Please include this as part of your Heplisav drug product release specifications.
9. The request to remove the (b) (4) test from the release tests of Heplisav is not acceptable. This was also stated in an e-mail on September 26, 2012. Please include this test as part of release and provide the revised Heplisav drug product testing plan to the BLA.
10. The reference material (b) (4) is to be requalified every (b) (4). It is not apparent that you have performed this requalification every (b) (4). Please provide this data.
11. Please clarify if the (b) (4) test will be used for analysis of the 1018 adjuvant as information related to this test is still present in section 3.2.5.2.4 (page 29) and 3.2.5.2.4.3.4 (page 35).
12. You indicate that you do not intend to perform post-approval stability analysis of the (b) (4). Because the (b) (4) method is being proposed to replace the (b) (4) methods, please provide purity/impurity stability data for the (b) (4) obtained using the (b) (4) method to support the proposed (b) (4) hold time. If adequate stability data using the (b) (4) method is not available for our review, please submit a post-approval stability protocol and commitment to collect these data for the (b) (4).
13. Please indicate where the SOP for the 1018 ISS concentration by (b) (4) (QTM-000289) document can be found.

Kind regards,

Katherine

RECORD OF TELEPHONE CONVERSATION

Katherine Berkousen
CAPT., US Public Health Service

FDA/CBER/Office of Vaccines
Div. of Vaccines & Related Products Applications
10903 New Hampshire Ave. WO71-3022
Silver Spring, MD 20993-0002