

(System Info - 213577 BERKHOUSEN KATHERINE 09/20/2012 12:46:55
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RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125428/0 Office: OVRR

Product: Hepatitis B Vaccine (Recombinant)

Applicant: Dynavax Technologies Corporation

Telecon Date/Time: 06-Aug-2012 09:28 AM Initiated by FDA? Yes

Communication Categorie(s): Information Request

Author: RICHARD DAEMER

Summary:

IR # 5 Request for establishment info: storage, manufacturing process, container closure systems

FDA Participants: Richard Daemer

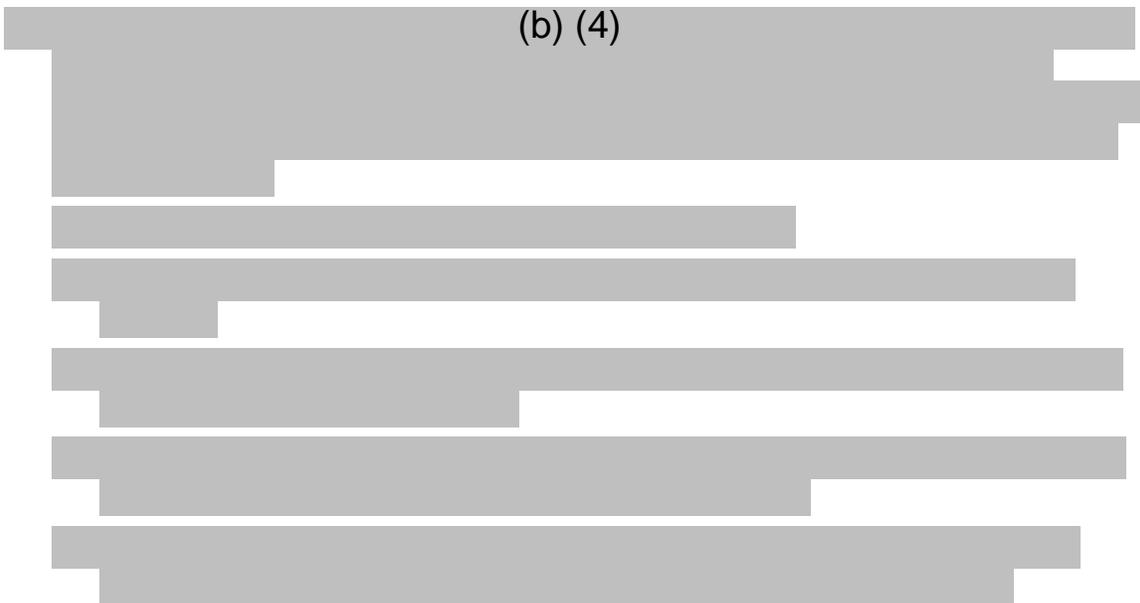
Non-FDA Participants: Elaine Alambra and William Turner

Telecon Body:

Email communication to Dynavax to request the following information:

With respect to the Drug Substance:

(b) (4)



(b) (4)

With respect to the final drug product:

1. With respect to filling of the final drug product, you state that a “target extractable (b) (4) is monitored...” Is this process a fill (b) (4) check? If not, please describe this procedure in greater detail.
2. You have described (b) (4) final formulation and fill process. Please clarify if you currently prepare intermediate final formulation volumes, or plan to in the future.
3. With respect to container closure integrity testing (CCIT), please provide the following:
 - a. A justification of your choice of (b) (4) challenge organisms. Please note that the organisms you have chosen are not generally considered worst case with respect to organism size.
 - b. Clarification if you utilized extremes of pressure during CCIT testing.
 - c. Results of post testing growth promotion tests for the growth medium.
 - d. The aperture size of positive controls utilized during testing.
4. In Table 7 of the FMEA report for Heplisav Drug Product Manufacture, you list a bioburden in process specification of (b) (4) (process). Please confirm that this is an actual in-process test to be performed routinely. If so, this in-process specification should be amended or removed, as bioburden found (b) (4) failure that should be investigated.
5. Please submit complete information regarding your final drug product 100% visual inspection program, to include the final defect test set, validation of the program, qualification of inspectors.
6. In Table 3.2.P.3.5–18: Step (b) (4) Capping Evaluation, you list a Container Closure integrity test that has been performed on vials filled using the (b) (4) batch size. Please completely describe this test, and state why this test was not performed for the (b) (4) batch size.
7. With respect to cleaning validation, please provide/respond to the following:
 - a. A listing and brief description of all non single use product contact equipment, and please re-state that all product contact equipment is dedicated.

- b. Complete cleaning validation final reports. These reports should include sufficient detail, such as swab locations, configurations of equipment within wash loads, etc.
 - c. Your chosen cleaning validation acceptance criteria for (b) (4) are not stringent enough for cleaning validation studies for final fill equipment, and also do not appear to meet your process capability, base on the validation data submitted in the BLA. Please explore holding a teleconference with CBER/DMPQ to discuss your cleaning validation program.
8. Please provide the results of media fills performed in support of filling of Heplisav, or results of media fills that have been performed using either the same vials used to fill Heplisav, or results of media fills that you believe to be supportive of use of the final Heplisav container configuration.
9. Please submit your SOP for media fills.