

RECORD OF TELEPHONE CONVERSATION

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

Product:
Hepatitis B Vaccine (Recombinant), Adjuvanted

Applicant:
Dynavax Technologies Corporation

Telecon Date/Time: 11-Apr-2013 12:00 AM Initiated by FDA? Yes

Telephone Number:

Communication Category(ies):
1. Meeting Communications - Additional

Author: KATHERINE BERKHOUSEN

Telecon Summary:
Response to CMC questions in the meeting request packet

FDA Participants: Katherine Berkhousen, Richard Daemer, Marian Major

Non-FDA Participants: William Turner, Elaine Alambra

Telecon Body:
A secure email was sent to the sponsor as per below:

From: Berkhousen, Katherine
Sent: Thursday, April 11, 2013 12:21 PM
To: 'Turner, William'; Alambra, Elaine
Cc: Major, Marian; Daemer, Richard J.; Berkhousen, Katherine
Subject: Response to Items 7 and 8 of the March 11, 2013 Dynavax Meeting Request
Importance: High

Dear Bill and Elaine,

Your amendment dated March 11, 2013, contained a meeting request and specific questions of which two were CMC questions. In our telecon with you on March 14, 2013 we denied your Type A Meeting request. We did agree to provide you with responses to items 7 and 8 (CMC questions) and item 9 (PNR) and to clarify any CMC issues if needed prior to any clinical discussions. We are providing you with our response to the CMC questions. Our response to the PNR was provided to you yesterday on April 10, 2013.

Response to Q7:

We do not agree that the submission of the final qualification/validation reports will demonstrate the acceptability of this equipment. You should submit final release data from final drug product lots manufactured after implementation of the new equipment. Data obtained from any three lots will be sufficient, provided your cleaning validation for the new (b) (4) and sterilization

validation for the new (b) (4) provide ample evidence that this equipment can clean and sterilize product contact equipment.

Response to Q8:

With reference to Section 9 of the Val-QC 113/089 Validation protocol and section 9.4 (Precision) of the Validation report: The intermediate precision for the in vivo potency assays were determined using data from three potency studies R03-021 to 023. In these studies you have stated that the Test article and Reference material were prepared from the same Heplisav DP batch (b) (4). In table 9-1 of section 9 of the validation protocol, you have proposed to establish precision, dose response and relative accuracy using the same material (b) (4) as reference and also as test article. The Validation Report, (section 9) shows the data generated by using the same drug product batch (b) (4) used as test article and as reference material. Your claim to have established the intermediate precision using the same DP batch (b) (4) as reference and also as test article is not acceptable. CBER expects a well characterized reference material and more than one lot/batch of DP to be used while performing validation studies.

More over, you have made reference to Retrospective study (Section 9.4 of the validation report) in support of intermediate precision. CBER currently does not accept the retrospective data in support of validation due to the reason that this data was not designed for the intended purpose and there were no set acceptance criteria established for performing such studies.

In your response above, you have stated that, "The validated assay has been used to perform Certificate of Analysis testing on (b) (4) lots confirming the suitability of the method for its intended use on multiple lots". Please provide the data and statistical analysis of these (b) (4) lots in comparison to a well characterized reference material, to support precision, and relative potency values.

Kind regards,

Katherine and Dick