

(System Info - 207079 DAEMER RICHARD 07/25/2012 16:00:37 DAEMER)

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: 18-Jun-2012 09:30 AM Initiated by FDA? Yes

Telephone Number:

Communication Category(ies):
1. Information Request

Author: RICHARD DAEMER

Telecon Summary:
Information request for statistical issues and SOP's

FDA Participants: Richard Daemer

Non-FDA Participants: William Turner

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

Please submit the following information to your BLA:

STATISTICAL

Please resubmit the data files after inserting in the currently submitted data the new variables as requested, and comment. This resubmission is important for an efficient reproduction of the submitted statistical results in your BLA.

1. ADAE.

This file includes 10,230 adverse events (AE) occurring to a total of 3449 subjects. Please insert the following additional variables on each of the existing AE records: visit

number (VISITNUM) and visit date -- at AE reporting; date of last injection prior to the current AE; treatment arm (ARMN) or treatment group (ACTARMN) as may be the case depending on the study protocol.

Also, the AE start dates were imputed ((I_AESTDT=Y) for 143 AEs. For the remaining (10,230-143) AEs, the AE start dates are reported as missing, although they are reported as treatment emergent AEs (AETRTEM=Y). This is a concern and reflects on the AE data quality. Please provide the imputing rules used.

2. ADLB with subsets ADLB10 and ADLB16. Please insert on each record the variables: date the visit took place, treatment arm (ARMN) and or treatment group (ACTARMN) as may be the case depending on the study protocol.

3. ADPIA. Please insert on each record the variables: treatment arm (ARMN) or treatment group (ACTARMN) as the case may be. The variables such as PIADTLS and ONGOINGC are mostly blank at present, please fill them in.

According to this file, in 125,470 instances the symptoms were reported as resolved (i.e., ONGOINGC=N). But the last symptom date (PIADTLS) was recorded only for 258 instances. Please retrieve the last symptom dates for all instances with resolved symptoms and insert back in file. Please also insert the dates as of which the symptoms in 695 instances (i.e. ONGOINGC=Y) were last found ongoing. Please explain the overwhelming majority of missing instances for these variables (PIADTLS and ONGOINGC).

4. ADSL/ADSL10/ADSL16. Please insert on each record the variables: visit number, VISLBL, and LRESULT and SRSLT1AN.

With regard to the variable Anti-HBsAg in the file, the (titer) values for 4392 subjects(55%) were not available out of a total of 7950 subjects in the file. Also, among subjects with available values (3558), a number of 3035 (85%) subjects had Anti-HBsAg=0.15. Please explain these percentages, 85% and 55%. Because the file documents do not apparently present brief introductory descriptions, please indicate, how these files differ or relate to the ADLB files in terms of purpose.

SOP's

5. In Table 2.7.2-5 (Section 2.7.2) the assays for measuring antibody to HBsAg are listed as the (b) (4). The SOP for anti-HBsAg testing in section 2.7.2 (SOP Q076D) describes the use of the (b) (4) kit, although it does not specify if this is the (b) (4). Please clarify.

There does not appear to be an SOP for the use of the (b) (4) kits. Please advise the location in the BLA of these SOPs describing the use of

the (b) (4) kits for testing anti-HBsAg antibodies or provide a copy of the SOPs.

6. The summary of the assay procedures submitted in the following SOPs are not detailed enough for reproduction of the tests in our labs for either in-support or lot release testing. Please provide complete SOPs.

SOP# QC152: Determination of 1018 ISS Identity by (b) (4)

SOP# A118: Determination of HBsAg Identity and (b) (4) for Heplisav Drug Product by (b) (4)

SOP# QC109: Determination of 1018 ISS Adjuvant Content in Heplisav Drug Product by the (b) (4) Assay

SOP# QC110: Determination of 1018 ISS Adjuvant (b) (4)

SOP# A090: Determination of HBsAg Protein Concentration in Heplisav Drug Product by the (b) (4) Assay

SOP# QC129: Determination of (b) (4) of HBsAg in Heplisav Drug Product by (b) (4)

SOP#s QC089 and QC113: In vivo (b) (4) Potency Assay