

RECORD OF TELEPHONE CONVERSATION

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

Product: Hepatitis B Vaccine (Recombinant), Adjuvanted

Applicant: Dynavax Technologies Corporation

Telecon Date/Time: 26-Jun-2013 10:00 AM Initiated by FDA? Yes

Telephone Number: 1-877-746-4263

Communication Category(ies):

1. Advice

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Telecon Summary:

Discussion with Dynavax regarding their proposed safety study

FDA Participants: Lorie Smith, Alexandra Worobec, Louis Schrager, Mridul Chowdhury, Marian Major, Katherine Berkousen, Richard Daemer

Non-FDA Participants: Elaine Alambra, William Turner, William Heyward, Robert Janssen, Edie Smith, (b) (4)

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body: CBER called Dynavax to inform them of 3 main points regarding their proposed safety study protocol prior to CBER's full formal comments. The main points conveyed were:

- 1) The proposed sample size (HEPLISAV 5000, Engerix-B 2500) was sufficient as long as it was an evaluable number of subjects. Therefore, attrition should be accounted for in enrollment calculations.

Dynavax stated that in previous studies, the safety population has been defined as any subject who received at least one vaccination and had any safety follow-up. For calculation purposes, Dynavax asked if there should be 5000 HEPLISAV subjects at the end of the study or if there should be 5000 subjects in the "safety population."

CBER responded that they would have to discuss this further internally. Otherwise, our response was agreeable to them.

2) CBER stated that the study would need to be "double-blinded."

- Dynavax noted that their prior studies had been "observer-blinded" which meant that an independent unblinded pharmacist administered the vaccine, but that the nurses/doctors/investigators and subjects remained blinded. CBER stated they did not think this would be a problem.
- There was some further discussion/questions regarding the rationale for not blinding and for blinding. See meeting outcome below.

3) CBER stated that that the primary objective would need to be changed from evaluating Wegener's to further evaluating the safety of HEPLISAV.

There was considerable discussion about powering a study for such an objective and for defining study success, etc. CBER reminded Dynavax that this is not a stand alone study to evaluate this objective, but an extension of the existing safety database and that perhaps viewing it as such will alleviate some of the statistical obstacles they were encountering. Dynavax had several questions regarding CBER's rationale and began discussing a lot of "nuts and bolts" details of the design and plan, much of which pertained to other comments we have and much of which had not yet been submitted in detail. CBER suggested that perhaps it would be more helpful for Dynavax to wait for CBER's final comments and review them in their totality. Some stated the some of Dynavax's questions within questions would be answered and a detailed discussion may be more productive once our comments were finalized and they have a chance to review them.