

(System Info - 221305 DAEMER RICHARD 12/12/2012 13:02:37 DAEMER)

**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: 26-Oct-2012 11:23 AM Initiated by FDA? Yes

Telephone Number:

Communication Category(ies):  
1. Information Request

Author: RICHARD DAEMER

Telecon Summary:  
Pharmacovigilance clarification

FDA Participants: None

Non-FDA Participants: None

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

1. In Section 1.16.10, the Sponsor proposed routine pharmacovigilance activities that would be performed by Dynavax or through a third-party contractor.
  - a. Please clarify how safety reports will be assessed and evaluated.
  - b. Please clarify if any analysis will be performed to detect a safety signal.
  - c. Please clarify if any adverse event of special interest will be closely monitored.

- d. Please clarify, in addition to case reports, if other sources of safety information will be sought and evaluated.
2. Safety data in pregnant women is considered to constitute important missing information. In Section 1.16.11, Table 1.16-18 stated that “A part of routine pharmacovigilance activities, all reports of exposure to HEPLISAV during pregnancy will be followed up to the outcome and will be recorded in the global safety database for HEPLISAV. Pregnancy data will be evaluated for safety signals.”
  - a. Please clarify how exposure to HEPLISAV during pregnancy will be captured.
  - b. Please clarify how pregnant women exposed to HEPLISAV will be followed up to the outcome using routine pharmacovigilance.
3. In Section 1.16.12, the Sponsor proposed to conduct a post-marketing observational safety study using a US HMO population. Table 1.16-19 stated that “the aim of the study is to assess the incidence of medically significant AEs, including autoimmune disease” and “the study population will consist of 5000 adults 18 years of age and older starting vaccination with HEPLISAV. A concurrent population of 5000 adults 18 years of age and older who initiated Engerix-B vaccination during the same period will be included for comparison.”
  - a. Please clarify what outcomes will be evaluated in the study, and especially, how autoimmune disease will be defined as one outcome or multiple outcomes.
  - b. Please clarify if the two cohorts will be matched or not. If matched, what are the matching factors?
  - c. Please clarify what you mean “during the same period”.
  - d. Please clarify what inclusion/exclusion criteria will be applied to the study population.
  - e. Please clarify if pregnant women will be included or excluded from the study.
  - f. Please clarify what dose(s) of HEPLISAV and Engerix-B will be evaluated.
  - g. Please clarify if any confounder and/or effect modifier will be considered.
  - h. Please provide an analysis plan.
  - i. Please clarify how the sample size, i.e., 5000 HEPLISAV recipients and 5000 Engerix-B recipients, was determined. nter details of telecon here]