

RECORD OF TELEPHONE CONVERSATION

Submission Information

Application Type	BLA
STN	125428/0.0
Review Office	OVRR
Applicant	Dynavax Technologies Corporation / Lic. # 1883
Product	Hepatitis B Vaccine (Recombinant), Adjuvanted
Trans-BLA Group:	No

Telecon Details

Telecon Date/Time	29-SEP-2017 05:30 AM
Author	AGNIHOTHRAM, SUDHAKAR
EDR	No
Post to Web	Yes
Outside Phone Number	
FDA Originated?	No
Communication Categories	IR - Information Request
Related STNs	None
Related PMCs	None
Telecon Summary	An IR with Questions about the Pharmacovigilance Plan DV-HBV-26
FDA Participants	Marian Major, Katherine Berkousen, Sudhakar Agnihothram and Richard Daemer
Applicant Participants	Elaine Alambra, Senior Director, Regulatory Affairs

Telecon Body:

From: Agnihothram, Sudhakar

Sent: Friday, September 29, 2017 5:33 PM

To: Elaine Alambra <EAlambra@dynavax.com>

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Cc: Berkhausen, Katherine <Katherine.Berkhausen@fda.hhs.gov>; Daemer, Richard J. <Richard.Daemer@fda.hhs.gov>

Subject: ** STN125428 - Request For Further Information - DV2 - HBV 26**

Dear Elaine,

We have the following comments on the protocol synopsis for study DV2-HBV-26 received on August 9th, 2017. Please provide a new draft version within **7 business days**.

1. As per the protocol synopsis, study DV2-HBV-26 will be conducted among 60,000 hepatitis B vaccinees (20,000 vs 40,000) from Kaiser Permanente Northern California (KPNC) and Kaiser Permanente Southern California (KPSC). Please clarify whether the decision to conduct Study HBV-25 only in KPSC impacts your plans for study sites for Study HBV-26 and if so, please update the protocol DV2-HBV-26 accordingly.
2. **Immune-mediated conditions.** You state under “Study Methods” that the pre-specified immune-mediated conditions were selected based on occurrence in previous HEPLISAV trials, common incidence, seriousness, or their ability to be diagnosed by objective, verifiable measures. Hence, you would investigate a total of 36 immune-mediated diseases in this study.
 - a. Please consider:
 - i. focusing mainly on immune-mediated granulomatous diseases and vasculitides
 - ii. adding all potentially immune-mediated conditions included in the list provided by the FDA and observed during the clinical trials including, but not limited to alopecia areata, cranial neuropathies, lichen planus, ulcerative proctitis, and vitiligo.
 - b. Under “Statistical Analyses” you state that *“As the immune-mediated adverse events may represent distinct biological pathways or etiologies, the analysis will be performed for each event separately”*
 - i. Please provide power calculations for each one of the events you are planning to investigate.
 - ii. In order to confirm/discard an association with immune-mediated diseases, a larger study would be necessary. Please provide the rationale for not conducting a larger study.
3. **Anaphylaxis.** You have included anaphylaxis (events of anaphylaxis occurring through 1 week after each injection) as an outcome.
 - a. Consider a shorter risk window following each injection, ideally day of vaccination.
 - b. Provide details on the statistical analysis.

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Please let us know if you have any questions.

Thanks,

Sudhakar

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