

# RECORD OF TELEPHONE CONVERSATION

## Submission Information

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

## Telecon Details

<b>Telecon Date/Time</b>	05-JUL-2017 06:20 PM
<b>Author</b>	AGNIHOTHRAM, SUDHAKAR
<b>EDR</b>	No
<b>Post to Web</b>	Yes
<b>Outside Phone Number</b>	
<b>FDA Originated?</b>	Yes
<b>Communication Categories</b>	IR - Information Request
<b>Related STNs</b>	None
<b>Related PMCs</b>	None
<b>Telecon Summary</b>	Pharmacovigilance IR requesting submission of revised Pharmacovigilance Plan
<b>FDA Participants</b>	Sudhakar Agnihothram, Katherine Berkousen and Richard Daemer. OVR/DVPA
<b>Applicant Participants</b>	Elaine Alambra, Senior Director Regulatory Affairs.

## Telecon Body:

**From:** Agnihothram, Sudhakar  
**Sent:** Wednesday, July 05, 2017 6:19 PM  
**To:** 'Elaine Alambra'  
**Cc:** Berkousen, Katherine; Daemer, Richard J.

## RECORD OF TELEPHONE CONVERSATION

**Subject:** Information Request STN 125428.0 - Requesting More Details on the Pharmacovigilance Plan

Dear Elaine,

Below, please find our request for further information regarding the proposed pharmacovigilance plan submitted in your BLA application.

### **Submission Information and Amendments Referred in this Information Request:**

**Risk Management Plan Version 2.0. BLA 125428/ SEQ No. 0072**

**Response to Information Request 8 May 2017. BLA 125428/ SEQ No. 0084**

**Response to Information Request 18 May 2017. BLA 125428/ SEQ No. 0088**

**Response to Information Request 7 June 2017. BLA 125428/ SEQ No. 0089**

- (1) You mentioned in your reply to question 5 of the information request dated on 7 June 2017 that you are planning to evaluate all emergency room and hospital events after vaccination to investigate the risk of medical events other than MACE outcomes and immune-mediated events following HEPLISAV vaccination. Given the observed timing of events such as MACE and herpes zoster in the HEPLISAV group, please justify why SCRI may be an appropriate approach to investigate medical events other than MACE and immune-mediated diseases, and/or propose alternative/additional study designs.
- (2) You initially planned to examine the risk of herpes zoster following HEPLISAV vaccination together with other medical events other than MACE outcomes and immune-mediated events. These medical events other than MACE outcomes and immune-mediated events would be identified from ER and hospital encounters. Herpes zoster is often diagnosed and treated in the outpatient setting. Have you planned to investigate the risk of herpes zoster following HEPLISAV vaccination also in the outpatient setting?
- (3) Please clarify whether you plan to investigate the risk of pre-specified immune-mediated events following HEPLISAV vaccination using both outpatient and inpatient data.
- (4) What is the average lag time between data entry and data availability for analysis in KPNC and KPSC. e.g. when would data collected in KPNC and KPSC as of December 31, 2017 be available for analysis?
- (5) Please submit an updated version of the Pharmacovigilance Plan including (1) updated sections related to “potential risks that require further investigation” (2) title, objectives and methods of the proposed post-marketing study according to all modifications discussed through the submitted and current information requests; (3)

## RECORD OF TELEPHONE CONVERSATION

updated power calculations for the outcomes to be investigated;; (4) follow-up time for each one of the for the outcomes to be investigated; (5) further details on how the safety of HEPLISAV in persons with HIV infection and chronic liver disease would be investigated in the proposed post-marketing surveillance study, (6) updated timelines for each one of the study components (cardiac events, immune-mediated diseases, herpes zoster, other medically attended events) including anticipated dates for:

- i) Final Protocol Submission
- ii) Study Completion
- iii) Final Report Submission

(6) Please provide a concept protocol of the pregnancy registry you are planning to conduct (Information Request dated on 23 June 2017).

Please provide your response by **COB 07/19/2017**.

Thanks,  
Sudhakar

Sudhakar Agnihothram B.Pharm, Ph.D,  
Primary Reviewer/ Regulatory Project Manager,  
Division of Vaccine Related Product Applications,  
Office of Vaccines Research and Review,  
Center For Biologics Evaluation and Research,  
10903, New Hampshire Avenue,  
BLDG 71, 3215 C,  
Silver Spring, Maryland, 20993.  
Email: [Sudhakar.Agnihothram@fda.hhs.gov](mailto:Sudhakar.Agnihothram@fda.hhs.gov)  
Ph: 301-348-3056