

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	18-MAY-2017 09:21 AM
Author	Silvia Perezvilar
EDR	No
Post to Web	Yes
Outside Phone Number	
FDA Originated?	Yes
Communication Categories	IR - Information Request
Related STNs	None
Related PMCs	None
Telecon Summary	IR Request via email - From Pharmacovigilance requesting more information on the Risk Management Plan
FDA Participants	Sudhakar Agnihothram, Katherine Berkousen, and Richard Daemer. RPMs- OVRR/DVRPA.
Applicant Participants	Elaine Alambra, Senior Director, Regulatory Affairs.

Telecon Body:

From: Agnihothram, Sudhakar
Sent: Thursday, May 18, 2017 3:17 PM
To: 'Elaine Alambra'

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Cc: Daemer, Richard J.; Berkhausen, Katherine

Subject: Request for Information Regarding Pharmacovigilance

Dear Elaine,

Please find our request for further information regarding the Risk Management Plan (RMP) version 2.0.

1. Feasibility of the proposed post-marketing safety study (page 55).
 - a. To clarify and support your estimation of accrual of 8,000 subjects per year, please provide the following information:
 - i. Most recent estimate of KPNC members ages 18 years or older eligible for Hepatitis B vaccination
 - ii. Most recent available Engerix-B coverage among KPNC members ages 18 years or older by year
 - iii. Most recent available coverage of each one of the potential comparator vaccines other than Engerix-B among KPNC members ages 18 years or older by year
 - iv. Potential plans for introduction of Heplisav in KPNC. What would be the decision-making process to select individuals who will receive either Heplisav or Engerix-B?
 - v. Any other information that you have used for this estimate
 - b. In case Heplisav uptake is lower than expected, do you have contingency plans to add data from additional databases?
2. On page 6 of the RMP you have stated “*Safety findings related to potential, adverse events of special interest (AESIs) in the TSP were analysed extensively. AESIs represent autoimmune, inflammatory and hypersensitivity disorders included in the list of AESIs provided to Dynavax by FDA*”. Nonetheless, the list of pre-specified immune-mediated events included in the proposed post-marketing study (page 58) does not include some of the potentially immune-mediated medical conditions included in the list provided by FDA.
 - a. Please justify the criteria used for such exclusions.
 - b. Please provide the list of ICD9 and/or ICD-10 codes of the events included the list of pre-specified immune-mediated events (page 58), as well as their respective background incidence rates (preferably from the US), together with the appropriate references for sources of data.
 - c. Please provide a list of immune-mediated diseases that may be related to TLR-9 together with the appropriate references.

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3. In regard to the study objective “*Comparison of the rates of 3-point Major Adverse Cardiovascular Events (MACE) during risk intervals with control intervals in Heplisav recipients*” (page 56). Please explain the scientific basis used to define the risk, non-risk and wash-out periods for MACE in the proposed SCRI analysis. Taking into account the results obtained in the HBV-23, please justify why SCRI would be appropriate and/or propose alternative study designs.
4. In regard to the study objective: “Comparison of the rates of medical events other than immune-mediated diseases or MACE during risk intervals with control intervals in HEPLISAV recipients” (page 56). Please specify to which medical events are you referring and why a self-controlled method would be appropriate for investigating those events. Have you planned to use an alternative study design if self-controlled methods are not appropriate?
5. On page 56 of the RPM, you have stated “*Patient accrual will begin following protocol approval by the FDA and KPNC. Following administration of Heplisav to the first patient in KPNC, patient accrual will continue until the prescribed KPNC utilization databases*”. Please clarify the methods planned for patient recruitment study (prospective?). Do your plans include request for informed consent? If so, what is your estimate for refusal to participate?

Please submit your response at your earliest convenience, and **no later than 5/26/2017**.

Thanks,

Sudhakar

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