

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	21-SEP-2017 3:00 PM
Author	AGNIHOTHAM, SUDHAKAR
EDR	No
Post to Web	Yes
Outside Phone Number	18777464263
FDA Originated?	Yes
Communication Categories	AD - Advice
Related STNs	None
Related PMCs	None
Telecon Summary	CBER Dynavax Telecon to discuss issues related to Pharmacovigilance plan
FDA Participants	CBER - Sudhakar Agnihothram, Silvia Perez-Vilar, Ruoxuan Xang, Amelia Horne, Deepa Arya, Craig Zinderman, Philip Krause, Marian Major, Scott Proestel, Richard Daemer, Katherine Berkousen, and Mridul Chowdhury.
Applicant Participants	Elaine Alambra, Graeme Curie, Rob Janssen, Randy Hyer, Biao Xing.

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Telecon Body:

As a follow up to the telecon on 09/15/2017, Dynavax indicated that they spoke to Kaiser Permanente Southern California (KPSC) to discuss the implementation of suggestions. As suggested in 9/15/17 telecon by CBER, Dynavax indicated to include the following suggestions to their Pharmacovigilance Plan.

- a. Additional Analyses of Unconfirmed MI's at the end of the study.
- b. Using the IPTW as the primary analytical approach.
- c. Providing Heplisav to additional 5000 patients.

To address the other suggestions made by CBER during the 9/21/17 telecon, Dynavax further indicated they are working Kaiser Permanente on addressing the following issues.

- a. Addressing the speed up of accrual
- b. Implementation of the additional vaccines in their system
- c. - Put in place a contingency plan to ensure complete accrual within the planned recruitment period.
- d. Inclusion of a recent historical cohort of hepatitis B vaccinees as secondary comparison group given the potential for selection bias with the concurrent hepatitis B cohort.

CBER further questioned Dynavax on how the Acute Myocardial Infarctions have been coded, and adjudicated. CBER further questioned Dynavax whether the diagnosis of the acute MI include cases of Coronary Artery Inflammation or the blockade of the stents, and other revascularization procedures. Dynavax responded that the classification will contain cardiac enzymes, EKG and MI symptoms, as was monitored in the HBV -23 study. CBER suggested that Dynavax include a detailed glossary of all - events that they will investigate and provide the definitions for confirmed cases and adjudicated cases.

There was a discussion around the usage of a point estimate of the Hazard Ratio of 2.5 for the interim analyses instead of ≥ 3.0 as proposed by Dynavax and ≥ 2.0 as proposed by CBER. CBER indicated that they will discuss this and will get back to Dynavax.