

RECORD OF TELEPHONE CONVERSATION

Submission Information

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

Telecon Details

Telecon Date/Time	24-MAY-2017 04:00 PM
Author	AGNIHOTHAM, SUDHAKAR
EDR	No
Post to Web	Yes
Outside Phone Number	1 (877) 746-4263
FDA Originated?	No
Communication Categories	AD - Advice
Related STNs	None
Related PMCs	None
Telecon Summary	Telephone call to Dynavax and CBER IOD regarding VRBPAC presentation; cardiac consult; labeling and PMC negotiations.
FDA Participants	Marion Gruber, OVRP/DVRPA Philip Krause, OVRP/DVRPA Marian Major, OVRP/DVP Wellington Sun, OVRP/DVRPA Katherine Berkousen, OVRP/DVRPA Richard Daemer, OVRP/DVRPA Sudhakar Agnihothram, OVRP/DVRPA

RECORD OF TELEPHONE CONVERSATION

Applicant Participants	Elaine Alambra, Senior Director, Regulatory Affairs Graeme Currie VP, Clinical Operations Robert Janssen VP, Clinical Research / Regulatory Affairs and Chief Medical Officer
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Telecon Body:

The following points were discussed during the teleconference.

Presentation of Clinical Safety Issues at VRBPAC

CBER indicated that the purpose of their call was to let Dynavax know that we continue to have a high level of concern regarding the cardiac events. Dynavax should be aware that the cardiac safety concerns will be a major topic that will be presented at VRBPAC. CBER will also be discussing other safety issues, to include autoimmune events, individual trial data and integrated safety data, but emphasis will be on the cardiac safety signals.

CBER encouraged Dynavax to present the clinical immunogenicity/effectiveness data of Studies 10 and 16 at the VRBPAC meeting as CBER will only be presenting a general summary for these studies and there are new members who have joined the VRBPAC committee since the 2012 VRBPAC. Therefore these new members will need to be informed on the immunogenicity data. CBER emphasized that they will not be focusing on the immunogenicity data at the VRBPAC.

Information requests

Dynavax questioned on whether CBER would be sending any additional information requests. CBER indicated that they will let Dynavax know by the mid of June.

Primary Safety Population

Dynavax questioned on whether their approach for following up on the primary safety population is reasonable. CBER indicated that they will not be able to comment on that during this telecon. CBER further added that since the trial design between the studies was different they will be discussing each of the individual studies (HBV 10, HBV 16 and HBV 23).

Other Safety Issues to be presented at VRBPAC

Dynavax questioned on whether CBER will be presenting any other safety issues at VRBPAC. CBER responded that the discussion will also be focused on Adverse Events of Special interests that include Tolosa-Hunt Syndrome and Wegener's Granulomatosis, which was discussed during the previous VRBPAC of 2012. CBER further indicated that CBER plans to discuss all of the safety issues that were listed in the CR letter dated November 10, 2016. Dynavax further indicated that they were planning to discuss Common Adverse Events and Medically Attended Adverse Events (which were also

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discussed by Dynavax at 2012 VRBPAC), and requested CBER`s input on the same. CBER`s response was for Dynavax to draft these data in 1 or 2 backup slides and present them if time permits.

Discussion on Vaccine Effectiveness

Dynavax indicated that they will present the risk/benefit analysis of the use of Heplisav and will make the case for the benefit of the use of vaccine. CBER acknowledged Dynavax`s comments. In addition, CBER indicated that they do not foresee any questions coming up on the discussion of effectiveness but discussion of effectiveness will be important in assessing the risk/benefit of the vaccine. CBER furthermore stated that considering the issues regarding the Severe Adverse Events observe, FDA will hold strong considerations on the decision of the VRBPAC to weigh the risk/benefit of this vaccine.

Post Marketing Studies

Dynavax questioned on whether CBER needs any further clarifications regarding the post marketing plans proposed by Dynavax, and CBER indicated that they have received the Dynavax`s response to the latest IR sent by the Pharmacovigilance team and the review is ongoing. CBER will reach out to Dynavax in the event if CBER needs any further details.

FDA External Consult Reports

Dynavax questioned CBER on whether they had approached any external consultants and CBER responded that they have consulted three cardiologists to seek their opinion on the cardiac safety signals. Dynavax requested CBER to send these reports, and CBER agreed to send the redacted versions of the external consults. CBER asked Dynavax if they had obtained any consults on the cardiac issues and Dynavax responded that they did not have any written reports per se. They had been working with cardiologists on their MACE analysis but they had no reports in writing.

Dynavax asked if CBER was going to supplement the VRBPAC with experts on cardiac issues and CBER responded that there would be cardiologists on the panel.

Labeling Negotiation

CBER conveyed their concern about the time crunch since the time between the VRBPAC and the action due date is very short, the labelling negotiations might take time. Dynavax acknowledged this. Dynavax asked if they could do as much as possible to cover other areas of the label that are less questionable ahead of VRBPAC and stated that they understood this would be done with no expectation of a decision. CBER responded that we would consider this as an approach.

The telecon concluded at 4:45 PM EST.