



**FOOD AND DRUG ADMINISTRATION**  
**CENTER FOR BIOLOGICS EVALUATION AND RESEARCH**

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MEMORANDUM

**BLA REVIEW**

**DATE:** 11-01-2017

**FROM:** Iryna Zubkova, PhD, OVR, DVP  
Product reviewer

**SUBJECT:** STN# 125428/0.108  
Response to Information Request from October 27, 2017

Sponsor: Dynavax Technologies Corporation

Product: Hepatitis B Vaccine (Recombinant), Adjuvanted [Heplisav- B<sup>®</sup>]

**TO:** Richard J. Daemer, PhD  
Sudhakar Agnihotram, PhD  
Katherine Berkhausen, PhD

**THROUGH:** Marian Major, PhD  
Robin Levis, PhD  
Sara Gagneten, PhD

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**Introduction**

Heplisav-B consists of recombinant hepatitis B surface antigen (HBsAg) produced in yeast cells (*Hansenula polymorpha*) combined with a novel cytosine phosphoguanine (CpG) enriched oligodeoxynucleotide (ODN) phosphorothioate immunostimulatory adjuvant (CpG 1018 adjuvant). Heplisav-B is supplied as a 0.5 mL single-dose vial. The Drug Product is formulated and filled at Rentschler Biotechnologie GmbH, Laupheim, Germany and the filled vials are transported to (b) (4) for labeling and packaging.

Following continued review of the BLA the need of an identity test after labeling operations at (b) (4) was brought up with Dynavax during a teleconference on October 26<sup>th</sup> 2017. The sponsor was informed that according to the Code of Federal Regulations (21 CFR 610.14) the contents of a final container of each filling of each lot needs to be tested for identity after all labeling operations have been completed. Dynavax confirmed that no such identity testing is performed following labeling of the vials at (b) (4) and as a result of the teleconference, an information request (IR) was sent to the sponsor. This memo is a review of the sponsor's response to the CBER's IR.

## **Information Request**

The following comments were sent to the sponsor on October 27th, 2017 and the response was received on October 27<sup>th</sup>, 2017. The CBER comments are shown in bold with the sponsor's response following in regular type.

**As discussed during the telecon on October 26, 2017 the Code of Federal Regulations (21 CFR 610.14) require that the contents of a final container of each filling of each lot shall be tested for identity after all labeling operations shall have been completed. Currently Dynavax does not perform an identity test on the contents of the final labeled product produced at (b) (4) facilities.**

- 1. Please add an identity test to the Drug Product specifications in Section 3.2.P.5.1 of the BLA. This can be done by renaming Table 3.2.P.5.1-1 as "HepBisav-B Final Container Specifications" and adding a second table, Table 3.2.P.5.1-2 titled "Final Product (Labeled and Packaged) Release Specification" with the chosen identity test and the acceptance criterion. Please submit this revised section to the BLA.**

### **Response:**

As requested Section 3.2.P.5.1 was revised and an additional table (Table 3.2.P.5.1-2: Final Product (Labeled and Packaged) Release Specification) was added.

**Table 3.2.P.5.1–2: Final Product (Labeled and Packaged) Release Specification**

<b>Parameter</b>	<b>Test Method</b>	<b>Acceptance Criterion for Release</b>
HBsAg identity	(b) (4)	Confirmed
(b) (4)		

Response is found to be acceptable.

- 2. Please confirm that Dynavax commits to performing this test at Dynavax, Dusseldorf on representative samples from all final labeled lots generated at (b) (4) for distribution in the U.S.**

### **Response:**

Dynavax confirmed that representative samples from all final labeled lots generated at (b) (4) for distribution in the USA will be tested for HBsAg Identity at Dynavax GmbH (Dusseldorf, Germany).

## **Conclusion**

The response is acceptable.