

RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125428/0 Office: OVRR

Product:
Hepatitis B Vaccine (Recombinant)

Applicant:
Dynavax Technologies Corporation

Telecon Date/Time: 21-May-2012 12:00 AM Initiated by FDA? Yes

Telephone Number:

Communication Category(ies):
1. Other -

Author: RICHARD DAEMER

Telecon Summary:
We contacted William Turner at Dynavax to clarify that the BLA would have a standard review timeline and the reasons for denial of a priority review request.

FDA Participants: Richard Daemer, Katherine Berkhausen

Non-FDA Participants: William Turner

Related STNs: None

Related PMCs: None

Telecon Body:

Bill,

As per our phone call with you this should clarify our rationale for denying the Priority Review based upon your criteria for justification.

1. Increased effectiveness in adults aged 18 to 70:

Although robust antibody levels were seen with HEPLISAV when administered to healthy adults and type II diabetics, the pivotal phase 3 trials (DV2-HBV-10 and -16) in BLA 125428/0000 were not designed as superiority studies against Engerix-B.

Accordingly, comparative claims cannot be made concerning the potential superiority of HEPLISAV efficacy in protecting against hepatitis B infection as compared to Engerix-B. Additionally, any hepatitis vaccine that results in seroprotection (defined as: anti-hepatitis B surface antigen antibody levels at 10 mIU/mL or higher) is deemed effective

for prevention of hepatitis B (*Hepatitis B, Red Book, 28th Edition, American Academy of Pediatrics, 2009, 337-356*). Therefore, antibody levels above the seroprotective level of 10 mIU/mL do not afford greater protection against hepatitis B, negating a claim of increased effectiveness of HEPLISAV as compared to existing hepatitis B vaccines.

2. Documented enhancement of patient compliance:

Although HEPLISAV is administered as a two-dose regimen while the currently licensed hepatitis B vaccines are administered as three dose regimens, a shorter regimen is not *prima facie* evidence of increased patient compliance with the regimen. No assessments comparing patient compliance with HEPLISAV and Engerix-B were submitted with this BLA. Accordingly, a request for priority review based on a claim of increased patient compliance cannot be supported.

3. Demonstration of safety and effectiveness in a new subpopulation (Type II diabetes mellitus):

While Dynavax provided evidence of safety and effectiveness in subjects with Type II diabetes, existing hepatitis B vaccines also have been shown to be safe and effective in this population. Currently, both Engerix-B and Recombivax are available for the prevention of hepatitis B in both healthy and immunocompromised individuals, including persons with Type II diabetes. Accordingly, a request for priority review based on this claim is not supportable.

Conclusion:

A request for priority review of the HEPLISAV BLA submission based on claims of increased effectiveness in adults aged 18 to 70, documented enhancement of patient compliance, or demonstration of safety and effectiveness in a new subpopulation (Type II diabetes mellitus), as set forth in CBER SOPP 8405, is not supported by the information provided in the BLA submission.

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