



DBSQ/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125814/0

From Seth Schulte, M.S.
Laboratory of Microbiology, *In-Vivo* Testing and Standards (LMIVTS)
Division of Biological Standards and Quality Control (DBSQ)

Through Maryna Eichelberger, Ph.D., Director, DBSQ
James L. Kenney, D.Sc., Chief, LMIVTS

Applicant Merck Sharpe & Dohme LLC (Merck)

Subject Biologics License Application (BLA): Review of bioburden, endotoxin, and sterility analytical methods used for pneumococcal 21-valent conjugate vaccine (CAPVAXIVE)

Recommendation: Approval

Executive Summary

The bioburden, endotoxin, and sterility analytical methods used for testing and release of CAPVAXIVE and the associated analytic method qualifications were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion

The analytical methods and their qualifications reviewed for CAPVAXIVE (b) (4) drug product were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe control of (b) (4) Drug Product (DP) (3.2.S.4 and 3.2.P.5, respectively), including descriptions of (b) (4) DP specifications, analytical procedures of (b) (4) DP, and qualifications of these analytical procedures were reviewed. In addition, the response to CBER's Information Request (IR) received on December 18, 2023 (Amendment #6) was also reviewed as mentioned below.

(b) (4)

One page has been determined to be not releasable: (b)(4)

(b) (4)

2. Endotoxin Method ((b) (4) DP)

Introduction

Endotoxin testing for (b) (4)
(b) (4) DP at MSD (b) (4) (MSD (b) (4)).

Specifications of (b) (4)
(b) (4) for DP must be met for release of CAPVAXIVE.

Method

The (b) (4) bacterial endotoxin test ((b) (4)-BET) used for (b) (4) DP is performed to quantitate bacterial endotoxins by (b) (4)

The (b) (4) bacterial endotoxin test ((b) (4)-BET) additionally used for DP is performed using (b) (4)

(b) (4)

The methods are described in more detail below together with the tests performed to determine the suitability of the test methods for their intended use.

(b) (4)

Endotoxin Qualification for DP

MSD (b) (4) qualified their (b) (4)-BET method for DP to determine if the method is suitable under the actual conditions of use. The test was performed using (b) (4) lots of DP (i.e., (b) (4)). The (b) (4) of DP was calculated to be (b) (4)

(b) (4)

MSD (b) (4) additionally qualified their (b) (4)-BET method for DP to determine if the method is suitable under the actual conditions of use. The test was performed using

the same lots with the same (b) (4) calculation as described under (b) (4)-BET qualification study above.

(b) (4)

Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product interference from (b) (4) DP test samples, thus indicating the (b) (4)-BET and (b) (4)-BET endotoxin test methods are appropriate under the actual conditions of use.

3. Sterility Method (DP)

Introduction

Sterility testing for DP is performed at MSD (b) (4) (MSD (b) (4)). Specification of 'No growth' must be met for release of CAPVAXIVE.

Method

(b) (4)

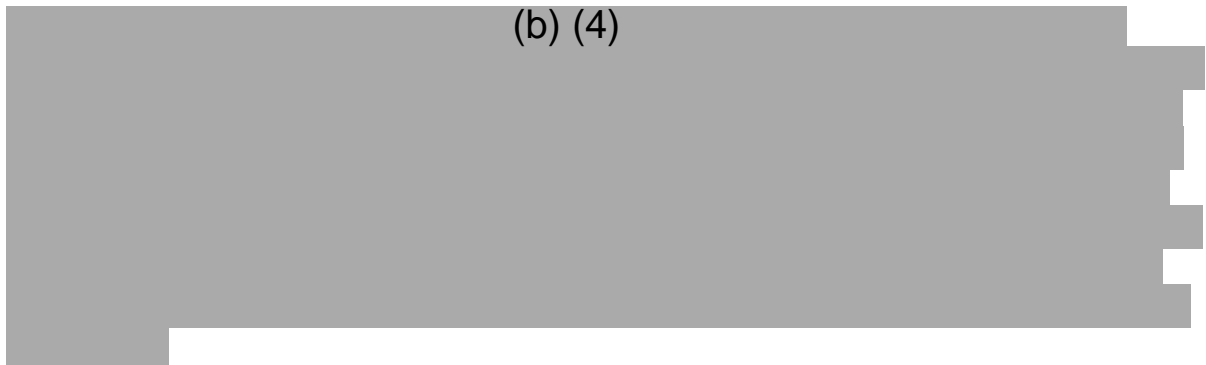
The method is described in more detail below together with the tests that were performed to determine suitability of the test method.

Sterility Qualification for DP

MSD (b) (4) qualified their (b) (4) method for DP by performing (b) (4) qualification studies to determine if the method is suitable under the actual conditions of use. The test was performed using (b) (4)

The test for each microorganism was performed using (b) (4)

(b) (4)



Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product interference from DP test samples, thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use.