DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

CBER REGULATORY REVIEW MEMORANDUM

Date 04 January, 2017

From Simleen Kaur, M.S.
Laboratory of Microbiology, *In-Vivo* Testing and Standards (LMIVTS)
Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To Biologics License Application Submission Tracking Number # 125614/0

Subject BLA: Review of Sterility and Endotoxin Test Methods for Herpes Zoster Vaccine, Shingrix®

Through James L. Kenney, D.Sc., Chief, LMIVTS
William M. McCormick, Ph.D., Director, DBSQC

Applicant Glaxo Smith Kline (GSK)

Product Shingrix®

Biologics License Application (BLA) Submission Tracking Number (STN) 125614/0

Submission Received by CBER 21 October, 2016

Review Completed 04 January, 2017

Material Reviewed
Method qualifications for: 1) sterility; and 2) endotoxin tests performed on Shingrix®. In addition, information request response received 18 November and 21 December of 2016 were reviewed.

Executive Summary
After a thorough review of this BLA, this reviewer finds the sterility, and endotoxin test methods were qualified in accordance with (b) (4) , respectively.

Background
On 21 October, 2016, GSK submitted this BLA for Shingrix®, a non-live recombinant vaccine indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older. Shingrix® is a sub unit vaccine consisting of recombinant varicella zoster virus glycoprotein E (gE), as an antigen combined

with adjuvant system $AS01_B$. The lyophilized gE protein and liquid adjuvant $AS01_B$ are provided in monodose vials of 50 µg/dose and 0.5mL/dose, respectively.

The DBSQC reviews BLAs and their supplements to ensure analytical methods are appropriate, properly validated and the product matrix is suitable for the intended test method. DBSQC also reviews release specifications for microbial and endotoxin testing to ensure they reflect process capability and meet regulatory compliance. These review activities support DBSQC's lot-release mission: the confirmatory testing of submitted product samples; review of manufacturers' lot-release protocols to ensure biological products are released according to licensed test methods and product specifications. Therefore, this review will focus on the following method qualifications for GSK's sterility and endotoxin test methods to ensure the product matrix is suitable for these intended test methods.

Review

Sterility Test Qualification for Shingrix® Drug Product (b) (4), final container and adjuvant $AS01_B$

GSK qualified their Shingrix® (b) (4) and final container and adjuvant $AS01_B$ matrixes using the (b) (4) qualification studies to demonstrate the matrixes are suitable for the intended test method. The test was performed using (b) (4)

(b) (4)

(b) (4)

thus indicating the Shingrix (b) (4) and final container and adjuvant $AS01_B$ are suitable for testing via their (b) (4) sterility test method.

(b) (4) Method Qualification for Shingrix® (b) (4) DP final container

GSK qualified their (b) (4) method for Shingrix® (b) (4) DP to verify their product matrixes are suitable for the intended test method in accordance with (b) (4).

(b) (4)

(b) (4)

(b) (4)

GSK submitted the endotoxin results for several (b) (4) DP lots, which met their endotoxin test specification of not more than (b) (4) protein and (b) (4) , respectively. CBER finds these proposed specifications acceptable.

Conclusions

After a thorough review of the information submitted in this BLA, this reviewer finds GSK's Shingrix® matrix is suitable for testing using their sterility and endotoxin testing methods; these tests were qualified and performed in accordance with (b) (4) and (b) (4) , respectively. Therefore, this reviewer finds these methods acceptable for their intended purpose.