Application Type	Original BLA
STN	125614/0
CBER Received Date	October 21, 2016
PDUFA Goal Date	October 20, 2017
Division / Office	DVRPA/OVRR
Committee Chair	Carmen Collazo-Custodio, PhD
Clinical Reviewer(s)	Paula Agger, MD MPH; Rebecca Reindel, MD
Project Manager	Ramachandra Naik, PhD; Michael Smith, PhD
Priority Review	No
Reviewer Name(s)	Rong Fu, PhD
Review Completion Date / Stamped Date	
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Applicant	GlaxoSmithKline Biologicals
Established Name	Zoster Vaccine Non-Live
(Proposed) Trade Name	Shingrix
Pharmacologic Class	Vaccine
Formulation(s), including Adjuvants, etc	After reconstitution, each 0.5 mL dose contains 50 μg of gE recombinant protein, 50 mcg of MPL and 50 mcg of QS-21.
Indication(s) and Intended Population(s)	Prevention of herpes zoster (shingles) in adults aged 50 years and older. By preventing herpes zoster, Shingrix reduces the overall incidence of postherpetic neuralgia.

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GLOSSARY

DoE	Design of Experiment
FC	Final Container
HZ	Herpes Zoster
IC	Internal Control
(b) (4)	
RSD	Relative Standard Deviation
RV	Reconstituted Vaccine
SD	Standard Deviation
(b) (4)	
SOP	Standard Operating Procedure

1. EXECUTIVE SUMMARY

GSK is seeking licensure of the herpes zoster (HZ) vaccine Shingrix (also referred to as HZ/su), indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older. This review focuses on the validation of an (b) (4) used 1) to determine the identity and gE content for (b) (4) samples of HZ/su, and 2) to determine the identity and dosage of gE antigen as a release and stability test for (b) (4) final container (FC), and reconstituted vaccine (RV). Overall, the validation data appear to support the intended use of the (b) (4) in each of these manufacturing steps.

2. CLINICAL AND REGULATORY BACKGROUND

Shingrix is a sub-unit vaccine consisting of the recombinant Varicella Zoster Virus glycoprotein gE as antigen combined with GSK's proprietary Adjuvant System AS01B. The same (b) (4) method is used to determine the identify and gE content of HZ/su for in-process samples and (b) (4) FC, and RV samples.

3. SOURCES OF DATA AND OTHER INFORMATION CONSIDERED IN THE REVIEW

3.1 Review Strategy

This review summarizes the validation approaches and results for the gE (b) (4) used in different manufacturing steps of HZ/su.

3.2 BLA/IND Documents That Serve as the Basis for the Statistical Review

The following documents submitted to STN 125614/0 m3.2.R were reviewed:

- Analytical method validation report: Improvement of the (b) (4) used for the identification of gE antigen and gE antigen content by (b) (4) in Hz/su vaccine in process sample (Report 9000036619 RVM002_001 Version 02).
- Analytical method validation report: Validation of the (b) (4) used for the identification and dosage of gE antigen by (b) (4) in gE (b) (4) gE final container, and Hz/su vaccine (Report 9000014481 RVM002_001 Version 03).

In addition, I also reviewed the information in STN 125614/0.35 m1.11, which included the applicant's response to CBER's information request dated July 24, 2017 regarding the gE ELISA assay.

4. DISCUSSION OF INDIVIDUAL ASSAYS

4.1 Validation of gE (b) (4) for use in (b) (4) samples

Several changes were made to the (b) (4) method used for (b) (4) samples (including (b) (4) after the initial validation. Complementary validation was therefore performed on the optimized method to assess the assay performance regarding trueness, precision, linearity, and range, and to establish new (b) (4). The validation followed the method procedure described in SOP 9000036619 (translation 9000040158 version 02).

(b) (4)

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(b) (4)

4.2 Validation of gE (b) (4) for use in (b) (4) FC, and RV steps

The validation followed the method procedure SOP 9000014481 (translation SOP 9000037069 version 03). The validation results are summarized below.

(b) (4)

4 pages have been determined to be not releasable: (b)(4)