Our STN: BL 125614/0 **BLA APPROVAL**

GlaxoSmithKline Biologicals
Attention: Jody Gould, Ph.D. October 20, 2017
14200 Shady Grove Road
VR1500
Rockville, MD 20850

Dear Dr. Gould:

Please refer to your Biologics License Application (BLA) for Zoster Vaccine Recombinant, Adjuvanted dated October 21, 2016, submitted under section 351(a) of the Public Health Service Act (PHS Act).

We have approved your BLA for Zoster Vaccine Recombinant, Adjuvanted effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Zoster Vaccine Recombinant, Adjuvanted under your existing Department of Health and Human Services U.S. License No. 1617. Zoster Vaccine Recombinant, Adjuvanted is indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT00434577, NCT00492648, NCT00802464, NCT00920218, NCT01086449, NCT01165177, NCT01165203, NCT01165229, NCT01295320, NCT01751165, NCT01777321, NCT01827839, NCT01954251 and NCT02075515.

Under this license, you are approved to manufacture Zoster Vaccine Recombinant, Adjuvanted. The lyophilized varicella zoster virus glycoprotein E (gE) antigen component and the $AS01_B$ adjuvant suspension component of the vaccine will be manufactured and filled at GlaxoSmithKline Biologicals S.A., located in (b) (4), Belgium. The lyophilized gE antigen component and $AS01_B$ adjuvant suspension component will be labeled and packaged at GlaxoSmithKline Biologicals S.A., located in (b) (4) Belgium and (b) (4) GlaxoSmithKline Vaccines, located in (b) (4)

You may label your product with the proprietary name SHINGRIX. The vaccine will be supplied in two different package configurations. One package configuration contains ten single-dose vials of gE antigen and ten single-dose vials of adjuvant. The other package configuration contains one single-dose vial of gE antigen and one single-dose vial of adjuvant.

DATING PERIOD

The dating period for the gE antigen and $AS01_B$ adjuvant components of Zoster Vaccine Recombinant, Adjuvanted shall be 36 months from the date of manufacture when stored at 2 °C to 8 °C. The dates of manufacture of the gE antigen and $AS01_B$ adjuvant components shall be defined as the dates of filling into final containers. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The expiration date for the packaged product, lyophilized gE antigen component and $AS01_B$ adjuvant suspension component, shall be dependent on the shortest expiration date of any component.

COMPARABILITY PROTOCOLS

This approval also includes comparability protocols for (b) (4) Under 21 CFR 601.12(e), approval of a comparability protocol may justify a reduced reporting category for a particular change. In your annual report (21 CFR 601.12(d)), you should report information confirming that the changes meet the requirements specified in your approved comparability protocol. Include the information described in 21 CFR 601.12(d)(3).

In addition, this approval includes a third comparability protocol for the qualification of (b) (4) Under 21 CFR 601.12(e), approval of a comparability protocol may justify a reduced reporting category for a particular change. You should report information confirming that the change meets the requirements specified in your approved comparability protocol as a **Supplement – Changes Being Effected in 30 Days** (21 CFR 601.12(c)). You should include the information described in 21 CFR 601.12 (b)(3) in this supplement. Although you may distribute the product made using this change 30 days after FDA receives the supplement, continued use of the change will be subject to our final approval of the supplement.

FDA LOT RELEASE

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you

must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of Zoster Vaccine, Recombinant, Adjuvanted, or in the manufacturing facilities.

LABELING

We hereby approve the draft package insert labeling submitted under amendment 56, dated October 18, 2017, and the draft carton and container labeling submitted under amendment 56, dated October 18, 2017.

Please provide your final content of labeling including the carton and container labels in Structured Product Labeling (SPL) format. All final labeling should be submitted as Product Correspondence to this BLA 125614 at the time of use (prior to marketing) and include implementation information on Form FDA 356h.

In addition, please submit the final content of labeling (21 CFR 601.14) in SPL format via the FDA automated drug registration and listing system, eLIST, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80), and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports for Vaccines* at http://www.fda.gov/forindustry/electronicsubmissionsgateway/ucm387293.htm. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable as the estimated annual number of pediatric herpes zoster cases is low and widely dispersed across the United States.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitments as described in your submission of October 18, 2017, to conduct the studies as outlined below:

1. Study Zoster-062 to assess the safety, reactogenicity and immunogenicity of SHINGRIX in adults ≥50 years of age with a prior episode of Herpes Zoster.

   Final Protocol Submission: June 30, 2018

   Study Completion: November 30, 2020

   Final Report Submission: November 30, 2021

2. A targeted safety study, EPI-ZOSTER-030 VS, to evaluate the safety of SHINGRIX in adults ≥50 years of age in the United States.

   Final Protocol Submission: January 30, 2019

   Study Completion: June 30, 2024

   Final Report Submission: March 30, 2025

3. Study Zoster-049 to assess the long-term efficacy, immunogenicity and safety of SHINGRIX in adults ≥50 years of age.

   Final Protocol Submission: December 18, 2015

   Study Completion: July 28, 2023

   Final Report Submission: May 25, 2024

Please submit clinical protocols to your IND 13857, and a cross-reference letter to this BLA 125614, explaining that these protocols were submitted to the IND.

If the information in the final study report supports a change in the labeling, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence**
- **Postmarketing Commitment – Final Study Report**
- **Supplement Contains Postmarketing Commitment – Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biological products qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely yours,

Marion F. Gruber, Ph.D.
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research