RECORD OF TELEPHONE CONVERSATION

Submission Information

Application Type	BLA
STN	125614/0.0
Review Office	OVRR
Applicant	GlaxoSmithKline Biologicals / Lic. # 1617
Product	Zoster Vaccine Recombinant, Adjuvanted

Telecon Details

Telecon Date/Time	29-AUG-2017 11:24 AM
Author	NAIK, RAMACHANDRA
FDA Originated?	Yes
Communication Categories	IR – Information Request
Telecon Summary	CBER's comments and request for additional information regarding GSK's Pharmacovigilance Plan
FDA Participants	Carmen Collazo-Custodio, Michael Smith and Ramachandra Naik
Applicant Participants	Jody Gould and Norris Pyle

Telecon Body: CBER’s e-message and the attachment for CBER’s comments/IR pasted below.

RECORD OF TELEPHONE CONVERSATION

From: Collazo, Carmen
Sent: Tuesday, August 29, 2017 11:24 AM
To: Jody Gould (jody.a.gould@gsk.com)
Cc: Norris Pyle (norris.h.pyle@gsk.com); Smith, Michael (CBER); Naik, Ramachandra
Subject: STN 125614/0 ~SHINGRIX~ CBER's comments regarding your Pharmacovigilance Plan (PVP)
Importance: High
Sensitivity: Confidential

Dear Dr. Gould,

Attached please find CBER's comments regarding your Pharmacovigilance Plan (PVP). Please confirm that you received this communication.

Regards,

Carmen

Carmen M. Collazo-Custodio, Ph.D.
Microbiologist (Team Leader)

Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
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RECORD OF TELEPHONE CONVERSATION

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH
OFFICE OF VACCINES RESEARCH AND REVIEW
DIVISION OF VACCINES AND RELATED PRODUCTS APPLICATIONS

DATE: **August 29, 2017** **PAGES:** **3**

TO: **GlaxoSmithKline Biologicals, S.A.**
Jody Ann Gould, Ph.D.
Sr. Director
US Lead, Zoster
North American Regulatory Affairs
FAX: (240) 238-9822 **Telephone: (610) 917-2985**

FROM: **Division of Vaccines and Related Products Applications**
Office of Vaccines Research and Review
Point of Contact: Carmen M. Collazo, Ph.D.
10903 New Hampshire Ave., White Oak Bldg. 71
Silver Spring, MD 20993-0002
FAX: (301) 595-1124 **Telephone: (301) 796-2640**

STN: **STN 125614/0**

PRODUCT: **SHINGRIX (Zoster Vaccine Recombinant, Adjuvanted)**

SUBJECT: **CBER comments regarding your Pharmacovigilance Plan (PVP)**

Dear Dr. Gould:

Our review of the information provided in your BLA dated October 21, 2016, for Zoster Vaccine Recombinant, Adjuvanted, is ongoing. We have the following comments regarding your responses received on July 27, 2017 (Amendment 31), and the subsequent summary of the proposed changes to the PVP received on August 11, 2017, that address CBER's Information Request dated June 30, 2017:

1. Please update the PVP in the Risk Management Plan based on the feedback provided in this communication and in accordance with established guidelines: (http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2E/Step4/E2E_Guideline.pdf).

2. **Regarding PVP routine surveillance**

We find your proposal for routine pharmacovigilance of inflammatory ocular and osseous pathology satisfactory. We recommend that you update the PVP to identify "Ocular neurovascular and vascular pathology leading to disturbances in visual acuity," and "Osseous pathology that may be due to inflammation" as separate important potential risks in the PVP so that these events can be monitored and analyzed separately from other pIMDs that are grouped together and were previously identified as a potential risk. Please provide information regarding the conditions you will include in these potential risk categories, and the specific MedDRA PTs or SMQs that you will use to identify cases.

3. Regarding enhanced surveillance

We agree with your proposal for enhanced surveillance of the 13 conditions that you identified (i.e., polymyalgia rheumatica, rheumatoid arthritis, psoriasis, autoimmune thyroiditis, multiple sclerosis, Guillain-Barré syndrome, idiopathic thrombocytopenia, optic neuritis, inflammatory bowel diseases, temporal arteritis, Still's disease adult onset, leukocytoclastic vasculitis and gout). Please also include cases of optic ischemic neuropathy and severe visual disturbances such as blindness in this list of conditions.

The follow-up questionnaires you propose will help gather data systematically for any reported cases. When available, please submit the questionnaire templates that you plan to use for CBER review, and submit the specific MedDRA PTs or SMQ that you will use to identify cases of the conditions identified above.

4. Regarding the Targeted Safety Study

We find your proposal for a Targeted Safety Study (TSS) to be acceptable, and suggest that you proceed with it as a postmarketing commitment. We have the following comments on your proposal:

a. <u>Study enrollment and data collection</u>:

i. You plan to conduct a non-interventional (observational) prospective cohort study. Please clarify whether the study will collect any data prospectively, or if the analysis will be retrospective, and only utilize data that is readily available in the database.

ii. Given the greater incidence of some of the conditions of concern (optic ischemic neuropathy and temporal arteritis) in an older population, please consider enriching your study population with individuals at higher risk.

iii. Please provide information on how you plan to identify and exclude subjects previously vaccinated with Zostavax from your study using electronic databases.

iv. You specified a study population consisting of 60,000 vaccinated individuals. Once you determine the specific study setting, please provide an estimate of the amount of time it would take for these vaccinations to accrue within the health system's database. Also, please estimate the number of vaccinations anticipated in one year in the selected health system.

b. Outcome identification:

i. You mention that ocular neurovascular and vascular pathology and osseous pathology will be included in Medically-Attended Adverse Events (MAEs). You also identify the following conditions that will be monitored, even if they are not MAEs: psoriasis, rheumatoid arthritis, inflammatory bowel diseases, autoimmune thyroiditis, idiopathic thrombocytopenia, optic neuritis, leukocytoclastic vasculitis, multiple sclerosis, Guillain-Barré syndrome, and Still's disease (adult onset). Please consider also including optic ischemic neuropathy and acute onset blindness in the list above.

ii. Please clarify how you plan to validate the study's ability to identify cases. For example, will you utilize validated case-definitions that exist in published literature, or will you evaluate the sensitivity and specificity, and/or the positive predictive value of methods you utilize to identify conditions of interest?

iii. Please comment on methods or approaches that may help increase the likelihood of identifying incident rather than prevalent cases.

c. Study design:

i. We acknowledge that you are assessing the feasibility of a design that incorporates a comparison group. You state in the statistical methods section that appropriate analyses will be performed. You also mention an observed to expected analysis based on background incidence rates from literature, or a within subject comparison with a historical baseline, and a self-controlled case series. For temporal arteritis, optic ischemic neuropathy and acute onset blindness, we encourage you to include a comparison group in the study design.

ii. If a signal is identified, please indicate if you plan to conduct a medical record review to assess the cases and conduct a confirmatory analysis.

Please provide your responses to this Information Request by September 6, 2017, in an Amendment to STN 125614/0. We recommend that you restate each item and follow it with your explanation or clarification. Use of this format helps organize the relevant information and provides a self-contained document that facilitates future reference. If

you have any questions about this communication, please contact Carmen M. Collazo, Ph.D. at (301) 796-2640.