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	19-SEP-2017 9:00 AM
Author	NAIK, RAMACHANDRA
FDA Originated?	Yes
Communication Categories	AD - Advice
Telecon Summary	Discussed GSK's preliminary thoughts/proposals regarding the Targeted Safety Study (TSS) and to confirm that GSK understands CBER's expectations to help the development of the study proposal.
FDA Participants	Paula Agger, Steve Anderson, Carmen Collazo-Custodio, Karen Farizo, Rong Fu, Ravi Goud, Ramachandra Naik, Douglas Pratt, Scott Proestel, Wellington Sun and Elizabeth Sutkowski
Applicant Participants	Emmanuelle Espié, Senior Epidemiology Lead Zoster, R&D Clinical and Epidemiology Jody Gould, Senior Director, Regulatory Affairs, North American Region Jacqueline Miller, Vice President and Head, US Clinical R & D Lidia Oostvogels, Director, Clinical and Epidemiology Project Leader Herpes Zoster Vaccine, Clinical RDC Belgium Harry Seifert, Senior Director, Pharmacovigilance Alliance, Vaccine Clinical Safety & Pharmacovigilance Jens-Ulrich Stegmann, Vice President, Head, Clinical Safety and Pharmacovigilance Fernanda Tavares, Director, Head of Safety Evaluation and Risk Management Catherine Cohet, Senior Epidemiology Expert, R&D Clinical and Epidemiology Kimber Poffenberger, Vice President, Head, North American Regulatory Affairs Veronique Bianco, Biostatistics

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Telecon Body:
At the beginning of the telecon, GSK asked for clarification regarding 'identification of outcomes', specifically vasculitis and inflammation, listed in the CBER's comments sent on September 18, 2017. CBER stated that our September 18, 2017, comments were specific to the Pharmacovigilance Plan (PVP) submitted to the BLA in the amendment 40 (dated September 7, 2017), and do not address the active surveillance targeted safety study (TSS). CBER understands the broad etiology and potential for an extensive list of conditions. Therefore, clinical judgement should be utilized to determine which conditions belong in this category. Our main concern is optic ischemic neuropathy, both arteritic and non-arteritic. GSK expressed their concern regarding collecting all ischemic, inflammatory, and broad terms for collecting both partial and complete blindness/neuropathy events, and provided the historic example of pandemic influenza, where collecting all events with visual loss was labor-intensive, and ultimately did not have much utility. GSK wishes to be judicious in providing data to CBER, so they will work with CBER regarding terminology that are clinically relevant. CBER clarified that the intention was to identify some specific terms, and conduct a qualitative analysis, and asked for clarification on GSK's seeming plans for more detailed disproportionality analyses. CBER stated that it is routine practice to do a qualitative analysis of similar cases to identify potential patterns/signals of interest. CBER and GSK both agreed on this plan/proposal for analysis of ocular complications in the PVP.

Regarding the TSS, GSK asked what the objectives should be. CBER replied that its recommendations regarding objectives of the TSS are listed in the CBER's comments [items 3(b)(i)-(iii)] sent to GSK on August 29, 2017. GSK asked for clarification regarding specific meaning of 'signal detection', and if CBER is interested in sequential analysis for signal detection. For example, GSK looks for specific events (like gout), and they asked if CBER is interested in incidence or relative risk. CBER replied that we recommend some sort of comparator utilizing a cohort or self-controlled methodology that could provide information regarding possible association with the vaccine. GSK stated that they have 3 approaches – (1) to include a comparator, (2) analysis of incidence, and (3) perform statistical analysis using a self-controlled case series. CBER stated that GSK's proposal for the TSS is acceptable, and requested GSK to send details.

CBER asked GSK if they have laboratory data regarding uric acid levels. If they do not have that information, can they conduct such study with already collected/stored sera samples? GSK stated that they don't have information on uric acid levels, and the existing frozen serum may be suboptimal to detect uric acid. CBER acknowledged.

Regarding the datasets or database, GSK stated that they are considering PRISM, and asked for CBER's perspective. CBER stated that PRISM may have a data lag, and it may take 3-5 years to do a study, and PRISM does not capture information very well for subjects over 65 years of age. Therefore, for subjects over 65 years of age, GSK may have to consider CMS. GSK could get access to this data, or conduct a study in these databases through the Reagan-Udall foundation, or Research Data Assistance Center (ResDAC). CBER suggested that one needs to be able to differentiate between

ZOSTAVAX and SHINGRIX vaccination, and asked GSK if a CPT code for SHINGRIX is in place. GSK stated that they are not aware of it, and this will be investigated.

Finally, GSK asked if CBER agrees with GSK's plan to submit both the responses to item 4 (regarding TSS) on August 29, 2017, IR, and to the August 18, 2017 IR regarding the PVP on Monday (September 25, 2017). CBER agreed.

Telecon ended.