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	03-AUG-2017 11:01 AM
Author	Ramachandra Naik
FDA Originated?	No
Communication Categories	Information request
Telecon Summary	GSK's response (sent as attachment to an e-mail message) to CBER's 8/1/2017 request to clarify error in reporting optic ischaemic neuropathy
FDA Participants	Carmen Collazo-Custodio, Ramachandra Naik and Michael Smith
Applicant Participants	Norris Pyle and Jody Gould

TELECON BODY:
GSK submitted their response, to CBER's 8/1/2017 clarification question regarding error in reporting optic ischaemic neuropathy, as an attachment to an e-mail message. GSK's 8/3/2017 e-mail message (page 2) and the attachment response (page 4) are pasted below.

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From: Norris Pyle [mailto:norris.h.pyle@gsk.com]
Sent: Thursday, August 03, 2017 11:01 AM
To: Naik, Ramachandra
Cc: Collazo, Carmen; Smith, Michael (CBER); Jody Gould
Subject: RE: STN 125614/0: Clarification regarding error in reporting optic ischaemic neuropathy

Hello Dr. Naik,
Please find attached GSK's response clarifying the below discrepancy. Please let me know if you need anything further. Thank you - Norris

From: Naik, Ramachandra [mailto:Ramachandra.Naik@fda.hhs.gov]
Sent: Tuesday, August 01, 2017 11:51 AM
To: Jody Gould
Cc: Collazo, Carmen; Smith, Michael (CBER); Norris Pyle; Linda Kramer
Subject: STN 125614/0: Clarification regarding error in reporting optic ischaemic neuropathy

EXTERNAL

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 clarification comment:

In Amendment 31 (submitted on July 26, 2017), Section 1.1.1.1 (response to Question 1), you state "there were no subjects in the HZ/su or Placebo groups reporting the occurrence of serious or non-serious optic ischaemic neuropathy within the 30 day post-vaccination period". However, according to the dataset, one subject in the HZ/su group (PID 1513, Zoster-022) reported the occurrence of non-serious optic ischaemic neuropathy on Day 29 after Dose 2 which was medically attended. The occurrence of this event appears to be reflected in Table 212 of the Integrated Summary of Safety and Table 10.22 of the Zoster-022 Clinical Study Report. Please clarify this apparent discrepancy.

If you have any questions about this communication, please contact Ramachandra Naik, Ph.D. or Michael Smith, Ph.D. at (301) 796-2640.
Regards,
Ram

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CBER IR of 1 August 2017:

In Amendment 31 (submitted on July 26, 2017), Section 1.1.1.1 (response to Question 1), you state "there were no subjects in the HZ/su or Placebo groups reporting the occurrence of serious or non-serious optic ischaemic neuropathy within the 30 day post-vaccination period". However, according to the dataset, one subject in the HZ/su group (PID 1513, Zoster-022) reported the occurrence of non-serious optic ischaemic neuropathy on Day 29 after Dose 2 which was medically attended. The occurrence of this event appears to be reflected in Table 212 of the Integrated Summary of Safety and Table 10.22 of the Zoster-022 Clinical Study Report. Please clarify this apparent discrepancy."

The Company's response:

The Company acknowledges that there is an error in the response as indicated by CBER and that there is one subject in the HZ/su group (PID 1513 in study ZOSTER-022) who has reported the occurrence of non-serious optic ischaemic neuropathy on Day 29 after Dose 2.

In addition to the tables referenced by CBER, this event is also included in Table 36 of the Integrated Summary of Safety that the Company referenced in the response document. The statement is erroneous and should be updated as follows: *"there **was one subject in the HZ/su group** and ~~were~~ no subjects in the ~~HZ/su or~~ Placebo group~~s~~ reporting the occurrence of serious or non-serious optic ischaemic neuropathy within the 30 day post-vaccination period"*.

The narrative of this case has previously been provided to CBER in Section 3.4.5 of Submission Package 4, Sequence 0029. The event description, provided in that document, is indicative of a non-arteritic ischaemic optic neuropathy assessed as mild as per investigator and may be explained due to the medical condition of chronic hypertension.

Therefore, for the assessment of optic ischemic neuropathy there are 3 events overall, 1 non-serious event that was inadvertently omitted in the summary description and the 2 serious events that have been described. All 3 events were apparently non-arteritic (non-inflammatory) and occurred in female, elderly subjects with concurrent medical conditions which may explain the occurrence of the reported episode. Following the inclusion of this third event in the assessment, the Company considers that the available data does not suggest a safety signal related to optic ischaemic neuropathy and the proposal for monitoring this event in the post-licensure setting remains unchanged.

The Company would also like to take the opportunity to clarify that in Table 1 in the response to Question 1 (Amendment 31, submitted on July 26, 2017), for the subject with PID 29571 the time to onset of 17 days is linked to the report of diplopia. The time to onset for the report of optic ischaemic neuropathy was 47 days. These reports are summarised in the table below.

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Other ID	Subject ID	Dose Number	Date of vaccination	List of events PT	Event Onset Date	Time Between Last Dose /Primary Event
ZOSTER-022	29571	1	25-APR-2011	Diplopia,	12-MAY-2011	17 days
				Optic ischaemic neuropathy	11-JUN-2011	47 days