

RECORD OF TELEPHONE CONVERSATION

Submission Type: Original Application Submission ID: 125259/0 Office: OVRR

Product:

Human Papillomavirus Bivalent (Types 16 and 18) Vaccine, Recombinant

Applicant:

GlaxoSmithKline Biologicals

Telecon Date/Time: 29-JUL-2009 05:03 PM

Initiated by FDA? Yes

Telephone Number:

Communication Category(ies):

Advice

Author: HELEN GEMIGNANI

Telecon Summary:

Safety Endpoints for VRBPAC

FDA Participants:

Non-FDA Participants:

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

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**From:** Gemignani, Helen S

**Sent:** Wednesday, July 29, 2009 5:03 PM

**To:** 'nicholas.perombelon@gskbio.com'

**Cc:** 'Cynthia.A.D'Ambrosio@gsk.com'; 'Matt.Whitman@gsk.com'

**Subject:** RE: Safety endpoints for Cervarix in VRBPAC

We have made some suggestions, to the table below, for your consideration. In general, in addition to overall totals, consider having slides with age breakdowns.

**Summary table of safety endpoints in GSK's VRBPAC briefing document and slides**

Safety endpoint	Data set	Data lock-point	Age range (years)
Solicited symptoms	Studies reported in BLA	Depending on study	10-25
Unsolicited symptoms	Studies reported in BLA	Depending on study	10-25
New onset of autoimmune disorders	Studies reported in BLA	Depending on study	10-25
Deaths (Consider 10-25 and > 25 breakdown within total)	All clinical studies in which <i>Cervarix</i> has been administered	August 31, 2008	10-72
Other serious adverse events (consider 10-25 and > 25 yo breakdown within total)	All clinical studies in which <i>Cervarix</i> has been administered	August 31, 2008	10-72
Study discontinuations due to adverse events (consider 10-25 and > 25 yo breakdown within total)	Studies reported in BLA plus ongoing extension studies and HPV-009	August 31, 2008	10-72
Pregnancies and pregnancy outcomes (consider 10-25 and > 25 yo age breakdown within total)	Studies reported in BLA plus ongoing extension studies and HPV-009	August 31, 2008	10-72
Medically significant adverse events (consider 10-25 and > 25 yo age breakdown within total)	Studies reported in BLA and ongoing extension studies	August 31, 2008	10-72
MPL meta-analysis	HPV vaccines and AS04-containing vaccines (i.e. levels 1 and 2)	June 2007	-
Updated MPL meta-analysis (neuroinflammatory and musculoskeletal events)	HPV vaccines and AS04-containing vaccines (i.e. levels 1 and 2)	August 2008	-
Updated MPL meta-analysis with expert review (neuroinflammatory and musculoskeletal events)	HPV vaccines and AS04-containing vaccines (i.e. levels 1 and 2)	December 2007	-

**From:** nicholas.perombelon@gskbio.com [mailto:nicholas.perombelon@gskbio.com]

**Sent:** Sunday, July 26, 2009 4:53 PM

**To:** Gemignani, Helen S

**Cc:** Cynthia.A.D'Ambrosio@gsk.com; Matt.Whitman@gsk.com

**Subject:** Fw: Safety endpoints for Cervarix in VRBPAC

Dear Helen,

We are now nearing completion of our VRBPAC briefing document and advancing in the development of our slide presentation. During this preparation, we have been discussing internally the presentation of safety and reactogenicity data from our clinical development program. We realize that there is an extensive prelicensure safety database now submitted to the BLA and over the last 2 years, we have provided various endpoints using differing ranges of studies and different data lock-points. However, for the sake of clarity for the VRBPAC members, we would like to focus our safety presentation (see summary table ) and request CBER's opinion on this proposal.

In developing this proposal, we have taken into account the recent comments received on the draft label for Cervarix, therefore, we intend to present for solicited and unsolicited symptoms and for autoimmune disorders of new onset the proposed indicated age range of 10-25 year olds. However, for more general safety endpoints (such as deaths, other serious adverse events, study discontinuations and medically significant adverse events), we prefer to show the VRBPAC the most recent data available (August 31, 2008) in the largest data set available (see table below). For pregnancies and pregnancy outcomes, again we suggest using the most recent data lock point and the data set including the large phase III study HPV-009. With respect to the MPL meta-analysis, as the initial analysis performed in June 2007 includes all the CBER categories of disorders, we would present this but then show the results of the expert review for the updated analysis of neuroinflammatory and musculoskeletal events (data lock-point December 2007)

We look forward to CBER's perspective on this summary and hope that we can align with CBER on the data sets to be presented to the VRBPAC members.

Please don't hesitate to contact me [610-787-3763 (phone)], Matt [610-787-3726 (phone)] or Cindy [610-787-3752 ] if you need any further clarification.

Thanks and best regards,

Nicholas

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New onset of autoimmune disorders	Studies reported in BLA	Depending on study	10-25
Deaths	All clinical studies in which <i>Cervarix</i> has been administered	August 31, 2008	10-72
Other serious adverse events	All clinical studies in which	August 31,	10-72

	<i>Cervarix</i> has been administered	2008	
Study discontinuations due to adverse events	Studies reported in BLA plus ongoing extension studies and HPV-009	August 31, 2008	10-72
Pregnancies and pregnancy outcomes	Studies reported in BLA plus ongoing extension studies and HPV-009	August 31, 2008	10-72
Medically significant adverse events	Studies reported in BLA and ongoing extension studies	August 31, 2008	10-72
MPL meta-analysis	HPV vaccines and AS04-containing vaccines (i.e. levels 1 and 2)	June 2007	-
Updated MPL meta-analysis (neuroinflammatory and musculoskeletal events)	HPV vaccines and AS04-containing vaccines (i.e. levels 1 and 2)	August 2008	-
Updated MPL meta-analysis with expert review (neuroinflammatory and musculoskeletal events)	HPV vaccines and AS04-containing vaccines (i.e. levels 1 and 2)	December 2007	-