The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 112485 (HPV-059 PMS)

Title: Safety of GlaxoSmithKline (GSK) Biologicals' human papillomavirus (HPV)-16/18 vaccine Cervarix® when administered to healthy females according to the prescribing information in Korea.
Cervarix™ (HPV): GSK Biologicals' candidate HPV-16/18 vaccine.

Rationale: The purpose of this study was to assess the safety of the HPV vaccine when administered in healthy Korean females aged 10 to 25 years according to the prescribing information in Korea. This surveillance study is to be performed over 6 consecutive years with a follow-up duration for each subject of approximately 7 months.
This CTRS presents the results collected during the 3rd year of surveillance. Indeed, no actual case was recruited during the first two years of surveillance, and then no results could be produced. For the next years, the CTRS will be updated when additional data become available.

Phase: Post-Marketing Surveillance Study (PMS)

Study Period: 23 June 2010 to 03 March 2011 (3rd year of surveillance)

Study Design: Open, self-contained, non-comparative, multi-centre study.

Centres: 5 centres in Korea.

Indication: Immunisation of healthy female subjects aged 10 to 25 years against HPV infection.

Treatment:
The study group was as follows:

- HPV Group: subjects received 3 doses of the HPV vaccine.

The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6 month vaccination schedule.
Note: according to the prescribing information, if flexibility in the vaccination schedule is necessary, the second dose can be administered between 1 month and 2.5 months after the first dose.
Subjects who had received 1 or 2 doses of HPV vaccine prior to the start of the PMS could also be enrolled.

Objective:

- To assess the safety of HPV vaccine in at least 3000 healthy Korean female subjects, when administered according to the Prescribing Information.

Primary Outcome/Efficacy Variable:

- Occurrence of adverse events (AEs) reported during the 30-day period (Day 0 to Day 29) following any vaccination.
- Occurrence of any serious adverse events (SAEs) and SAE(s) causally related to vaccination reported throughout the PMS period (up to one month after the third vaccine dose).
- Occurrence of medically significant conditions throughout the PMS period (up to one month after the third vaccine dose) regardless of causal relationship to vaccination and intensity*.

Medically significant conditions were defined as: AEs prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases.
Common diseases included: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities and injury
*Note that the analysis was not performed for this outcome since it was not a requirement of the Korean regulatory authority.

Secondary Outcome/Efficacy Variable(s):
Outcome variables were not differentiated into primary and secondary in the study protocol; all are considered as primary outcome variables for this study.

Statistical Methods:
The analysis was performed on the Total Vaccinated cohort that included all vaccinated subjects with at least one dose of HPV vaccine administration documented.

Analysis of safety:
The percentage of subjects with at least one report of an adverse event (AE) during the 30-day period following any vaccination was tabulated according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms.
The SAEs collected during the whole year of the surveillance study were tabulated according to MedDRA preferred

terms.

Study Population: Healthy female subjects between, and including, 10 to 25 years of age at the time of first vaccination were enrolled in the study. Women of childbearing potential were not to be pregnant. Absence of pregnancy was to be verified (e.g. urine pregnancy test) as per the investigator's clinical judgment. Subjects were to have no contraindications according to the local approved prescribing information. Subjects should not have received more than 2 doses of the study vaccine outside this study and no previous vaccination with a HPV vaccine other than the study vaccine was allowed. Written informed consent (or assent in the case of subjects below the age of consent) was obtained from each subject, and also from a parent / legally acceptable representative in the case of subjects below the age of consent, prior to the performance of any study-specific procedures.

Surveillance Year 3:

Number of Subjects:	**HPV Group**
Planned, N	500
Randomised, N (Total Vaccinated cohort)	105
Completed, n (%)	94 (89.5)
Total Number Subjects Withdrawn, n (%)	11 (10.5)
Withdrawn due to Adverse Events, n (%)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable
Withdrawn for other reasons, n (%)	11 (10.5)
Demographics	**HPV Group**
N (Total Vaccinated cohort)	105
Females: Males	105:0
Mean Age, years (SD)	20.4 (3.72)
Korean, n (%)	104 (99.0)

Primary Efficacy Results: Number (%) of subjects with adverse events and with serious adverse events (Total Vaccinated cohort)
Please refer to the safety section of the document for these outcome variables.

Secondary Outcome Variable(s): Not applicable.

Safety results: Number (%) of subjects with adverse events during the 30-day period (Day 0 to Day 29) following any vaccination (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-29 following vaccination)	**HPV Group N = 105**
Subjects with any AE(s), n (%)	30 (28.6)
Injection site pain	19 (18.1)
Pyrexia	6 (5.7)
Headache	3 (2.9)
Injection site swelling	3 (2.9)
Nausea	3 (2.9)
Dizziness	2 (1.9)
Injection site erythema	2 (1.9)
Injection site induration	2 (1.9)
Injection site pruritus	2 (1.9)
Upper respiratory tract infection	2 (1.9)

Adverse events counting rule: > 30 subjects/treatment group and ≤ 3 groups in the study, the most frequent 10 events are to be listed.

Safety results: Number (%) of subjects serious adverse events reported up to one month after the third vaccine dose (Total Vaccinated cohort)

Serious adverse event, n (%) [n considered by the investigator to be related to study medication]

All SAEs	**HPV Group N = 105**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
Fatal SAEs	**HPV Group N = 105**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]

Conclusion:
During the 3rd year of surveillance, at least one AE was reported by 30 (28.6%) subjects in the HPV Group within the 30-day follow-up period after vaccination. No SAEs were reported during the 3rd year of this surveillance study.

Publications: None.

Date updated: 20-Sept-2011