

**Rapporteur's
Public Assessment Report
for paediatric studies submitted in
accordance
with Article 46 of Regulation (EC)
No1901/2006, as amended**

**POLIORIX
(Inactivated Poliomyelitis Vaccine)**

PL/W/0005/pdWS/001

**Marketing Authorisation Holder:
GlaxoSmithKline**

Rapporteur:	Poland
Start of the procedure (day 0):	26.11.2010
Date of this report:	03.02.2011
Deadline for Rapporteur's preliminary paediatric assessment report (PPdAR)(day 70):	04.02.2011
Deadline for CMS's comments:	19.02.2011
Finalisation procedure (day 90)	24.02.2011

ADMINISTRATIVE INFORMATION

Invented name of the medicinal product:	POLIORIX
INN (or common name) of the active substance(s):	Inactivated poliomyelitis vaccine
MAH:	GlaxoSmithKline
Currently approved Indication(s)	Poliorix™ is indicated for active immunisation from the age of 2 months against poliomyelitis.
Pharmaco-therapeutic group (ATC Code):	J 07 BF 03
Pharmaceutical form(s) and strength(s):	Solution for injection Vials of 0.5 ml dose of vaccine contains: 40 D antigen units of type 1 (Mahoney), 8 D antigen units of type 2 (MEF-1), 32 D antigen units of type 3 (Saukett) of the polio virus.
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I. EXECUTIVE SUMMARY

No SmPC and PL changes are proposed.

II. RECOMMENDATION¹

No changes in the product information are required. In addition, no further regulatory action or information is required.

III. INTRODUCTION

On 26 of November 2010, the MAH submitted four completed paediatric studies for Poliorix™, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended, on medicinal products for paediatric use.

A short critical expert statement for each study also has been provided.

The MAH stated that the submitted paediatric studies do not influence the benefit risk for Poliorix and that there is no consequential regulatory action.

IV. SCIENTIFIC DISCUSSION

IV.1 Information on the pharmaceutical formulation used in the studies

The pharmaceutical form of Poliorix™ used in presented trials were the same solution for deep intramuscular injection in vials of 0.5 ml – one dose of vaccine contains:

40 D antigen units of type 1 (Mahoney),
8 D antigen units of type 2 (MEF-1),
32 D antigen units of type 3 (Saukett) of the polio virus.

IV.2 Clinical aspects

1. Introduction

The MAH submitted four final reports for:

- **IPV –16 (108344 – June 2008)** “An open multicentric, post-marketing surveillance study to monitor the safety and reactogenicity of GlaxoSmithKline Biologicals Poliomyelitis Vaccine (inactivated) Poliorix™, administered in Korean children as a primary vaccination in healthy subjects aged two to six months or as a booster vaccination in subject aged four to six years”;
- **IPV-16(108344 – July 2009)** “An open multicentric, post-marketing surveillance study to monitor the safety and reactogenicity of GlaxoSmithKline Biologicals Poliomyelitis Vaccine (inactivated) Poliorix™, administered in Korean children as a primary vaccination in healthy subjects aged two to six months or as a booster vaccination in subject aged four to six years”;

¹ The recommendation from section V can be copied in this section

- **IPV-17** (112581) -“An open-label primary vaccination study to assess the safety and reactogenicity of GlaxoSmithKline Biologicals Inactivated Poliomyelitis Vaccine Poliorix™, administered as a three-dose primary vaccination course at 2, 3 and 4 months of age in healthy infants in China”;
- **IPV-19** (112683) - “An open-label primary vaccination study to assess the safety and reactogenicity of GlaxoSmithKline Biologicals Inactivated Poliomyelitis Vaccine Poliorix™, administered as a booster-dose at 18-24 months of age in healthy toddlers in China”

2. Clinical studies

IPV –16 (108344 – **June 2008**) “An open multicentric, post-marketing surveillance study to monitor the safety and reactogenicity of GlaxoSmithKline Biologicals Poliomyelitis Vaccine (inactivated) Poliorix™, administered in Korean children as a primary vaccination in healthy subjects aged two to six months or as a booster vaccination in subject aged four to six years”.

➤ **Description:**

This surveillance was the 2nd year surveillance conducted after POLIORIX vaccine registration in Korea (12 May 2006).

➤ **Methods**

The study collected safety data on POLIORIX administered as a primary vaccination in healthy subjects aged two to six months or as booster vaccination in subjects aged four to six years as per the regulations of Korean Food and Drugs Administration (KFDA) Data was collected through case report forms (CRFs)

➤ **Results**

212 subjects were enrolled, of which 205 subjects received the vaccine as a primary vaccination dose and 7 subjects received the vaccine as a booster dose. Of the 212 subjects, 112 subjects (52.8%) received one dose, 56 subjects (26.4%) received two doses of the vaccine and 44 subjects (20.8%) received three doses of the vaccine. None of the subjects were eliminated from analysis as the analysis was based on the total vaccinated cohort.

Pain and irritability were the most commonly reported solicited (expected) local and general symptoms, respectively. Unsolicited (unexpected) symptoms were reported by 15.1% of the subjects during the 7-day (Day 0 – 6) follow-up period and 40.1% of the subjects during the 31-day (Day 0 -30) follow-up period. Serious adverse events such as croup infections and pneumonia were reported but none was assessed to be causally related to vaccination.

Within the 31-day (Days 0-30) post-vaccination period no subjects reported symptoms that were assessed to be definitely related to vaccination. Symptoms that were assessed to be probably related, possibly related and of unknown causality to vaccination were reported by one subject each. No subjects reported symptoms of grade 3 intensity with causal relationship to vaccination.

IPV-16(108344 – **July 2009**) “An open multicentric, post-marketing surveillance study to monitor the safety and reactogenicity of GlaxoSmithKline Biologicals Poliomyelitis Vaccine (inactivated) Poliorix™, administered in Korean children as an primary vaccination in healthy subjects aged two to six months or as a booster vaccination in subject aged four to six years”.

➤ **Description:**

This surveillance was the 3rd year surveillance of the six-year analysis planned to be conducted after the POLIORIX vaccine registration in Korea (12 May 2006).

➤ **Methods**

The study collected safety data on POLIORIX administered as a primary vaccination in healthy subjects aged two to six months or as booster vaccination in subjects aged four to six years as per the regulations of Korean Food and Drugs Administration (KFDA). Data was collected through case report forms (CRFs).

➤ **Results**

137 subjects were enrolled, 136 subjects received the POLIORIX vaccine as a primary vaccination dose and one subject received the vaccine as a booster dose. Of the 137 subjects, 66 subjects (48.2%) received one dose, 27 subjects (19.7 %) received two doses of the vaccine and 44 subjects (32.1%) received three doses of the vaccine. None of the subjects were eliminated from analysis as the analysis was based on the total vaccinated cohort.

Redness and irritability were the most commonly reported solicited local and general symptoms, respectively. Unsolicited symptoms were reported for 16.1% of subjects during the 7-day (Days 0 - 6) follow-up period and 30.7% of subjects during the 31-day (Days 0 - 30) follow-up period. Serious adverse events such as pneumonia and pneumonia aspiration were reported but none were assessed by the investigator to be causally related to vaccination Grade 3 unsolicited symptoms were not reported for any of the subjects. None of the subjects were reported for unsolicited symptoms with causal relationship to vaccination, as assessed according to KFDA assessment and/or GSK assessment during the 31-day (Days 0-30) post-vaccination period.

IPV-17 (112581) -“An open-label primary vaccination study to assess the safety and reactogenicity of GlaxoSmithKline Biologicals Inactivated Poliomyelitis Vaccine Poliorix™, administered as a three-dose primary vaccination course at 2, 3 and 4 months of age in healthy infants in China”.

➤ **Description:**

Evaluation of safety and reactogenicity of primary vaccination with GlaxoSmithKline Biologicals' Inactivated *Poliomyelitis* Vaccine *Poliorix* administered in three-dose schedule at 2, 3 and 4 months of age in healthy infants in China.

➤ **Methods**

• Objective(s)

To assess the safety and reactogenicity of GSK Biologicals' IPV vaccine administered as a three-dose primary vaccination course.

• Study design

Open, single-group, single-centre study.

• Study population /Sample size

Healthy male or female subjects between, and including, 60 and 90 days of age at the time of the first vaccination were included in the study.

A total of 25 subjects were enrolled to the study. A total of 23 subjects completed the study.

• Treatments

All subjects except two received three doses of the GSK Biologicals' *Poliorix* vaccine, administered intramuscularly into the upper side of the right thigh.

• Outcomes/endpoints

Safety and reactogenicity after each vaccine dose:

- Occurrence of solicited local and general symptoms during the 4-day (Day 0-Day 3) follow-up period following each dose of the study vaccine.

- Occurrence of unsolicited symptoms during the 31-day (Day 0-Day 30) follow-up period following each dose of the study vaccine.
- Occurrence of serious adverse events (SAEs) from Dose 1 up to one month (minimum 30 days) following the last vaccination.

- **Statistical Methods**

All analyses were performed as specified in the protocol and/or study reporting and analysis plan (RAP).

The statistical analyses were performed using the Statistical Analysis Systems (SAS) version 9.1 on Windows XP Professional and StatXact-7.0 procedure on SAS.

➤ **Results**

- **Recruitment/ Number analysed**

Twenty five subjects were enrolled in this study. A total of 23 subjects completed the study. Two subjects withdrew from the study after receiving the first dose of the study.

Vaccine: the first one was withdrawn from the study after the administration of the first dose of vaccine on request of the parents- they withdrew consent. This consent withdrawal was not related to any AE/SAE.

The second one was withdrawn from the study after the administration of the first dose of vaccine because the investigator realized that the subject violated the exclusion criteria. The decision for withdrawal was made by the investigator and the infant's parents.

- **Baseline data**

The mean age of the subjects in the Total Vaccinated Cohort was 9.6 weeks with a standard deviation of 1.38 week. Female subjects constituted 60% of the study population. All the subjects vaccinated in the study were of Asian-Chinese heritage.

- **Safety results**

The safety analysis was performed on the Total Vaccinated Cohort. At least one symptom (solicited/unsolicited, local/general) was reported for 72% of subjects. The percentage of subjects for whom at least one Grade 3 symptom (solicited/unsolicited, local/general) was reported, was 8%. At least one symptom (solicited/unsolicited, local/general) that required medical attention was reported for 24% of subjects. Pain at injection site was the most frequently reported solicited local symptom during the 4-day (Day 0-3) follow-up period after vaccination, reported for 12% of subjects. There were no reports of Grade 3 solicited local symptoms. Irritability was the most frequently reported solicited general symptom, reported for 56% of subjects. It was also the only reported Grade 3 symptom, reported for two subjects. At least one unsolicited symptom during the 31-day (Day 0-30) follow-up period after vaccination was reported for 60% of subjects. No Grade 3 unsolicited symptoms or unsolicited symptoms with causal relationship to vaccination were reported for any of the subjects.

IPV-19 (112683) - "An open-label primary vaccination study to assess the safety and reactogenicity of GlaxoSmithKline Biologicals Inactivated Poliomyelitis Vaccine Poliorix™, administered as a booster-dose at 18-24 months of age in healthy toddlers in China".

➤ **Description:**

Evaluation of safety and reactogenicity of a booster dose of GlaxoSmithKline Biologicals' Inactivated *Poliomyelitis* Vaccine *Poliorix* administered at 18-24 months of age in healthy toddlers in China.

➤ **Methods**

- **Objective(s)**

To assess the safety and reactogenicity of a booster dose of GSK Biologicals' IPV in toddlers.

- **Study design**

Open, single-group, single-centre study in the People's Republic of China. All subjects received a single dose of the *Poliorix* vaccine at 18-24 months of age.

- **Study population /Sample size**

Healthy male or female subjects between, and including, 18 and 24 months of age at the time of the booster vaccination and who received three doses of Oral Polio Vaccine (OPV) as primary vaccination in the first year of life as per Chinese recommendations.

A total of 26 subjects were enrolled in this study. 25 subjects were vaccinated and completed the study.

- **Treatment**

All subjects received a single dose of the *Poliorix* vaccine at 18-24 months of age.

- **Outcomes/endpoints**

Safety and reactogenicity after vaccine dose:

-Occurrence of solicited local and general symptoms during the 4-day (Day 0-Day 3) follow-up period after the study vaccination.

- Occurrence of unsolicited symptoms during the 31-day (Day 0-Day 30) follow-up period after the study vaccination.

- Occurrence of serious adverse events (SAEs) following booster vaccination.

- **Statistical Methods**

All analyses were performed as specified in the protocol and/or study reporting and analysis plan (RAP).

The statistical analyses were performed using the Statistical Analysis Systems (SAS) version 9.1 on Windows XP Professional and StatXact-7.0 procedure on SAS.

➤ **Results**

- **Recruitment/ Number analysed**

A total of 26 subjects were enrolled in this study after checking the inclusion and exclusion criteria. A total of 25 subjects were vaccinated and completed the study. A total of 25 subjects were analysed.

- **Baseline data**

The mean age of the subjects was 20.3 months with a standard deviation of 1.49 months and female subjects constituted 52 % of the study population. All the subjects vaccinated in the study were of Asian-Chinese heritage.

- **Safety results**

The safety analysis was performed on the Total Vaccinated Cohort. At least one symptom (solicited/unsolicited, local/general) was reported for 48% of subjects. At least one symptom (solicited/unsolicited, local/general) that required medical attention was reported for 4% of subjects. There were no reports of Grade 3 (solicited/unsolicited, local/general) symptoms. Redness at the injection site was the most frequently reported solicited local symptom during the 4-day (Day 0-3) post-vaccination follow-up period, reported for 20% of subjects. There were no reports of Grade 3 solicited local symptoms.

Fever was the most frequently reported solicited general symptom, reported for 24% of subjects. No Grade 3 solicited general symptoms were reported for any of the subjects. At least one unsolicited symptom during the 31-day (Day 0-30) follow-up period after vaccination was reported for 40% of subjects. No Grade 3 unsolicited symptoms or unsolicited symptoms with causal relationship to vaccination were reported for any of the subjects.

V. RAPPORTEUR'S OVERALL CONCLUSION AND RECOMMENDATION

➤ Overall conclusion

Assessors received answers from Germany, Hungary and The Netherlands in time up to 90 day of procedure: there are no further comments.

No changes in the product information are required. In addition, no further regulatory action or information is required.

➤ Recommendation

No further action required.

VI. REQUEST FOR SUPPLEMENTARY INFORMATION

Not applicable.