In February 2013, GlaxoSmithKline (GSK) announced a commitment to further clinical transparency through the public disclosure of GSK Clinical Study Reports (CSRs) on the GSK Clinical Study Register.

The following guiding principles have been applied to the disclosure:

- *Information will be excluded in order to protect the privacy of patients and all named persons associated with the study*
- *Patient data listings will be completely removed* to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the **GSK Clinical Study Register**.*
- *Aggregate data will be included; with any direct reference to individual patients excluded*

**Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered*

This study includes documents that were originally reported in a language other than English. All documents that are available in English have been made available via the GSK Clinical Study Register.

Annual report for Post-Marketing Surveillance and Surveillance on particular patients groups (2nd year)

reporter	Company license No. (importer's number)	89		
reporter	name of manufacturer(business)	GlaxoSmithKline		
reporter	Address of manufacturer (Business)	191, Hangang-ro-2-ga, Yongsan-gu, Seoul, 140-702, Korea		
reporter	name	PPD	resident no.	PPD
manufacturer	name	GlaxoSmithKline	country	Belgium
manufacturer	address	89 Rue de 1 Institut, 1330, Rixensart, Belgium		
product on re-examination		Rotarix™	period of re-examination	07March 2008 - 06March 2014
approval no.		161	approval date	07 March 2008
surveillance results	period and no. of survey patients	Period: Total No. of subjects entered in the study: 877 subjects No. of subjects from whom surveillance reports were collected: 877 subjects No. of subjects in the Total Vaccinated cohort safety assessment: 876 subjects No. of subjects in efficacy assessment: None		
surveillance results	Result and analysis	Refer to the attached report		
Invoice Sales (shipment result)		Refer to the attached report		

I hereby report the annual report of the Post-Marketing Surveillance and special surveillance based on the Notice of New Drug Re-examination 7-1.

Date:

Reporter: PPD (stamped)
Manager: Director Clinical R&D and Medical Affairs: PPD (Bio-MD)
Telephone: PPD

To Korean Food & Drug Administration

Attached Document

fee

Attached Document
1 Safety data from results of domestic PMS.
2. Safety data on the occurrence of adverse events in domestic and foreign investigations other than 1.
3. Data reported regarding safety such as domestic and foreign literatures and academic informations
4. Data on selling in domestic and foreign countries and approval status in foreign countries.

Annual Report for Post-Marketing Surveillance and Surveillance on **Rotarix™**
(Oral live attenuated human rotavirus vaccine)

GlaxoSmithKline

[Annex 1] Overall of post-marketing surveillance

Type of post-marketing surveillance			No. of patients	Performance status and future protocol
post-marketing surveillance	General drug use surveillance		877	Any adverse event was reported for 630 subjects during the 31-day post-vaccination period.
	Special subgroup	Surveillance on children	876	
		Surveillance on elderly people	0	
		Surveillance on pregnant women	0	
		Surveillance on renal impairment patients	0	
		Surveillance on hepatic impairment patients	0	
		Surveillance on long-term use	0	
		Surveillance on other special patients	0	

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1. Post Marketing Surveillance Protocol

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3. General Information of PMS

3.1 Surveillance period

Rotarix™ vaccine was registered in Korea on 07 March 2008 and was launched in the same market in June 2008. This surveillance, in the first and second year after the Rotarix™ vaccine was registered in Korea, was conducted between September 2008 to December 2009. A total of 877 subjects were enrolled in the study of which 876 subjects were included in the Total Vaccinated cohort (TVC). One subject was eliminated from the analysis since for this subject the subject number was allocated but the study vaccine dose was not administered.

3.2 Subjects composition table [Appendix 2]

[Annex 2] Table of patient composition

No. of all survey patients from whom CRFs were collected. : 877 survey patients

No. of survey patients excluded from safety assessment : 1 survey patient

Reasons	No. of subjects
Used drug before contract	00
Failure of follow-up	00
Off label use (not meet indication)	00
No administration	01

No. of survey patients included in safety assessment : 876 survey patients

No. of survey patients excluded from efficacy assessment : Not Applicable

No. of survey patients included in efficacy assessment : Not Applicable

3.3 Summary table of PMS

Name of hospital	Name of doctor	CRF No.	Date of contract	Surveillance period	Collected cases
PPD			25August 2008	August 2008-December 2009	20
			09December 2008	December 2008-December 2009	18
			21November 2008	November 2008 - December 2009	20
			21October 2008	October 2008 - December 2009	30
			01September 2008	September 2008 - December 2009	20
			01 September 2008	September 2008 - December 2009	20
			01September 2008	September 2008-December 2009	30
			01 October 2008	October 2008 - December 2009	30
			16 October 2008	October 2008 - December 2009	11
			08 April 2009	April 2009 - December 2009	20
			18 September 2008	September 2008 - December 2009	20
			18 September 2008	September 2008 - December 2009	20
			26 September 2008	September 2008-December 2009	70
			26 September 2008	September 2008 - December 2009	30
			16 October 2008	October 2008-December 2009	20
			11 September 2008	September 2008 - December 2009	30
			11 September 2008	September 2008-December 2009	12
			18 September 2008	September 2008 - December 2009	13*
			19September 2008	September 2008 - December 2009	20
			11 September 2008	September 2008-December 2009	2
			25September 2008	September 2008-December 2009	20
			17 October 2008	October 2008-December 2009	30
			30 October 2008	October 2008-December 2009	20
			29 September 2008	September 2008-December 2009	10
			06 October 2008	October 2008 - December 2009	4
			12 December 2008	December 2008-December 2009	40

Name of hospital	Name of doctor	CRF No.	Date of contract	Surveillance period	Collected cases
PPD			27 November 2008	November 2008-December 2009	40
			29 September 2008	September 2008-December 2009	10
			29 September 2008	September 2008-December 2009	10
			26 December 2008	December 2008-December 2009	100
			21January 2009	January 2009 - December 2009	16
			21J anuary 2009	January 2009-December 2009	1
			18 November 2008	November 2008-December 2009	20
			29 October 2008	October 2008-December 2009	49
			05 December 2008	December 2008-December 2009	50
total					876

Collected cases = The number of subjects enrolled and the safety data was recorded in the CRF.
* One subject (subject No. PPD was enrolled in to the study but did not receive any dose of Rotarix™.

IV. Summary of PMS results

4. Summary of PMS results

4.1 Summary and objective of the drug use investigation

GlaxoSmithKline Korea has registered its oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ in Korea on 07 March 2008, following which, the present post-marketing surveillance (PMS) was conducted to collect reactogenicity and safety data on the use of Rotarix™ in at least 3000 Korean infants (approximately 500 infants to be enrolled every year for 6 years) as per the regulations of the Korean Food and Drugs Administration (KFDA). This surveillance, in the second year after the vaccine was registered in Korea, was conducted between September 2008 and December 2009 and presents the data from the first and second year of surveillance.

4.2 Demographic data

Table 1 presents the demographic data of subjects by age (weeks) and gender for the Total Vaccinated cohort.

Table 2 presents the demographic data of subjects by race and gender for the Total Vaccinated cohort.

Of the 876 subjects who received at least one dose of Rotarix™ documentation on age at the time of first dose was available for 875 subjects. The age of one subject (subject No. PPD was unknown. The number of male and female subjects was similar; 440 subjects were male and 436 subjects were female. The mean age of the subjects was 9.6 weeks (range: 4 to 24 weeks) with a standard deviation (SD) of 2.35 weeks (Table 1).

Majority of the subjects (874 subjects) were of Korean heritage. Two subjects were of Non-Korean (Chinese) heritage (Table 2).

Table 1 Demography data: Age* by Gender (Total Vaccinated cohort)

Group	Gender	N	N with age	MEAN	SD	MIN	MAX
HRV	F	436	435	9.5	2.32	6	24
	M	440	440	9.6	2.38	4	24
	Total	876	875	9.6	2.35	4	24

HRV = Human rotavirus vaccine
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age
*For the subjects who have received their Dose 1 of Rotarix™ prior to this study age was derived by considering the date of that vaccination.

Table 2 Demography data: Race by Gender (Total Vaccinated cohort)

Group	Race	Male N = 440	Female N = 436	Total N = 876
HRV	Korean	439	435	874
	Non-Korean	1	1	2

HRV = Human rotavirus vaccine
N = Total number of subjects in the mentioned category

4.3 Previous medical history

Table 3 presents the summary of previous medical history by gender, for the Total Vaccinated cohort.

Table 4 presents the previous medical history by classification for the Total Vaccinated cohort.

Overall 118 (13.5%) subjects had a previous medical history.

- A total of 42 (4.8%) subjects had a history of respiratory, thoracic and mediastinal disorders (acute bronchiolitis, acute bronchitis, acute nasopharyngitis, bronchitis, cough (common cold), nasal stuffy, nasopharyngitis, pneumonia, respiratory distress syndrome, streptococcal tonsillitis, upper respiratory infection (URI) and urinary tract infection (UTI)).
- A total of 33 (3.8%) subjects had a history of gastrointestinal disorders (acute gastritis, acute gastroenteritis (AGE), diarrhoea, gastroenteritis (GE), gastroesophageal reflux (GER), infantile colic, inguinal hernia, necrotizing entero-colitis (NEC), neonatal vomiting, non infectious neonatal diarrhea, R/O mild AGE and umbilical Hernia).
- A total of 26 (3.0%) subjects had a history of skin and subcutaneous disorders (allergic urticaria, atopic dermatitis, candidid, diaper rash, melanosis, neonatal omphalitis, non specific eczema, seborrheic dermatitis and unspecific rash).
- A total of 13 (1.5%) subjects had a history of eye disorders (acute conjunctivitis, conjunctivitis, eye discharge, neonatal conjunctivitis, R/O conjunctivitis and R/O nasolacrimal duct obstruction).
- A total of 11 (1.3%) subjects had a history of hepatobiliary disorders (jaundice and neonatal jaundice).
- A total of 11 (1.3%) subjects had a history of other disorders (breast milk jaundice, cleft lip and palate, intrauterine growth retardation and prematurity).
- A total of 7 (0.8%) subjects had a history of blood and lymphatic system disorders (anemia, neutropenia and sepsis).

Table 3 Previous medical history - by gender (Total Vaccinated cohort)

			Male N=440		Female N=436		Total N =876	
Group	**Previous medical history**	**Category**	**n**	**%**	**n**	**%**	**n**	**%**
HRV	ANY MEDICAL HISTORY	YES	60	13.6	58	13.3	118	13.5
		NO	380	86.4	378	86.7	758	86.5
	BLOOD AND LYMPHATIC SYSTEM	YES	2	0.5	5	1.1	7	0.8
		NO	438	99.5	431	98.9	869	99.2
	CARDIAC	YES	2	0.5	1	0.2	3	0.3
		NO	438	99.5	435	99.8	873	99.7
	EAR AND LABYRINTH	YES	3	0.7	1	0.2	4	0.5
		NO	437	99.3	435	99.8	872	99.5
	ENDOCRINE	YES	1	0.2	0	0.0	1	0.1
		NO	439	99.8	436	100	875	99.9
	EYE	YES	7	1.6	6	1.4	13	1.5
		NO	433	98.4	430	98.6	863	98.5
	GASTROINTESTINAL	YES	18	4.1	15	3.4	33	3.8
		NO	422	95.9	421	96.6	843	96.2
	HEPATOBILIARY	YES	5	1.1	6	1.4	11	1.3
		NO	435	98.9	430	98.6	865	98.7
	IMMUNE SYSTEM (INCL ALLERGIES, AUTOIMMUNE DISORDERS)	YES	0	0.0	1	0.2	1	0.1
		NO	440	100	435	99.8	875	99.9
	INFECTIONS AND INFESTATIONS	YES	1	0.2	0	0.0	1	0.1
		NO	439	99.8	436	100	875	99.9
	METABOLISM AND NUTRITION	YES	2	0.5	1	0.2	3	0.3
		NO	438	99.5	435	99.8	873	99.7
	NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS, POLYPS)	YES	1	0.2	0	0.0	1	0.1
		NO	439	99.8	436	100	875	99.9
	OTHER	YES	3	0.7	8	1.8	11	1.3
		NO	437	99.3	428	98.2	865	98.7
	RESPIRATORY, THORACIC AND MEDIASTINAL	YES	23	5.2	19	4.4	42	4.8
		NO	417	94.8	417	95.6	834	95.2
	SKIN AND SUBCUTANEOUS TISSUE	YES	15	3.4	11	2.5	26	3.0
		NO	425	96.6	425	97.5	850	97.0

HRV = Human rotavirus vaccine
N = Total number of subjects in each group (Male/female/Total)
n (%) = number (percentage) of subjects with the specified category (Yes/No)

Table 4 Previous medical history – by classification (Total Vaccinated cohort)

		HRV				
					95% CI	
Previous Medical History	Diagnosis Or sign Symptom	N+	n	%	LL	UL
BLOOD AND LYMPHATIC SYSTEM	ANEMIA	7	3	2.5	0.5	7.3
	NEUTROPENIA	7	1	0.8	0.0	4.6
	SEPSIS	7	3	2.5	0.5	7.3
CARDIAC	ASD. TR.	4	1	0.8	0.0	4.6
	ATRIAL SEPTAL DEFECT	4	1	0.8	0.0	4.6
	PUL. HTN	4	1	0.8	0.0	4.6
	TRICUSPID REGURGITATION	4	1	0.8	0.0	4.6
EAR AND LABYRINTH	ACUTE RHINITIS	4	1	0.8	0.0	4.6
	OTITIS EXTERNA	4	2	1.7	0.2	6.0
	OTITIS MEDIA	4	1	0.8	0.0	4.6
ENDOCRINE	HYPOTHYROIDISM	1	1	0.8	0.0	4.6
EYE	ACUTE CONJUNCTIVITIS	14	1	0.8	0.0	4.6
	CONJUNCTIVITIS	14	3	2.5	0.5	7.3
	EYE DISCHARGE	14	1	0.8	0.0	4.6
	NEONATAL CONJUNCTIVITIS	14	6	5.1	1.9	10.7
	R/O CONJUNCTIVITIS	14	1	0.8	0.0	4.6
	R/O NASOLACRIMAL DUCT OBSTRUCTION	14	2	1.7	0.2	6.0
GASTROINTESTINAL	ACUTE GASTRITIS	34	1	0.8	0.0	4.6
	AGE	34	8	6.8	3.0	12.9
	DIARRHEA	34	1	0.8	0.0	4.6
	GASTROENTERITIS	34	10	8.5	4.1	15.0
	GER	34	2	1.7	0.2	6.0
	INFANTILE COLIC	34	2	1.7	0.2	6.0
	INGUINAL HERNIA	34	1	0.8	0.0	4.6
	NEC (NECROTIZING ENTERO - COLITIS)	34	1	0.8	0.0	4.6
	NEONATAL VOMITING	34	1	0.8	0.0	4.6
	NON INFECTIOUS NEONATAL DIARRHEA	34	1	0.8	0.0	4.6
	R/O GASTROESOPHAGEAL REFLUX	34	1	0.8	0.0	4.6
	R/O GERD	34	1	0.8	0.0	4.6
	R/O MILD AGE	34	1	0.8	0.0	4.6
	UMBILICAL HERNIA	34	3	2.5	0.5	7.3
HEPATOBILIARY	JAUNDICE	11	3	2.5	0.5	7.3
	NEONATAL JAUNDICE	11	8	6.8	3.0	12.9
IMMUNE SYSTEM (INCL ALLERGIES, AUTOIMMUNE DISORDERS)	ALLERGIC PROCTOCOLITIS	1	1	0.8	0.0	4.6
INFECTIONS AND INFESTATIONS	LYMPHADENITIS	1	1	0.8	0.0	4.6
METABOLISM AND NUTRITION	NEONATAL JAUNDICE	3	3	2.5	0.5	7.3
NEOPLASMS BENIGN, MALIGNANT AND	NECROSIS OF SCROTUM	1	1	0.8	0.0	4.6

		HRV				
					95% CI	
Previous Medical History	**Diagnosis Or sign Symptom**	**N+**	**n**	**%**	**LL**	**UL**
UNSPECIFIED (INCL CYSTS, POLYPS)						
OTHER	BREAST MILK JAUNDICE	11	1	0.8	0.0	4.6
	CLEFT LIP AND PALATE	11	1	0.8	0.0	4.6
	INTRAUTERINE GROWTH RETARDATION	11	1	0.8	0.0	4.6
	PREMATURITY	11	8	6.8	3.0	12.9
RESPIRATORY, THORACIC AND MEDIASTINAL	ACUTE BRONCHIOLITIS	45	2	1.7	0.2	6.0
	ACUTE BRONCHITIS	45	3	2.5	0.5	7.3
	ACUTE NASOPHARYNGITIS	45	3	2.5	0.5	7.3
	BRONCHITIS	45	1	0.8	0.0	4.6
	COUGH (COMMON COLD)	45	1	0.8	0.0	4.6
	NASAL STUFFY	45	1	0.8	0.0	4.6
	NASOPHARYNGITIS	45	2	1.7	0.2	6.0
	PNEUMONIA	45	2	1.7	0.2	6.0
	RESPIRATORY DISTRESS SYNDROME	45	1	0.8	0.0	4.6
	STREPTOCOCCAL TONSILLITIS	45	1	0.8	0.0	4.6
	URI	45	25	21.2	14.2	29.7
	UTI	45	3	2.5	0.5	7.3
SKIN AND SUBCUTANEOUS TISSUE	ALLERGIC URTICARIA	27	1	0.8	0.0	4.6
	ATOPIC DERMATITIS	27	10	8.5	4.1	15.0
	CANDIDID	27	1	0.8	0.0	4.6
	DIAPER RASH	27	3	2.5	0.5	7.3
	MELANOSIS	27	1	0.8	0.0	4.6
	NEONATAL OMPHALITIS	27	3	2.5	0.5	7.3
	NON SPECIFIC ECZEMA	27	1	0.8	0.0	4.6
	SEBORRHEIC DERMITITIS	27	6	5.1	1.9	10.7
	UNSPECIFIC RASH	27	1	0.8	0.0	4.6

HRV = Human rotavirus vaccine
N+=Total Number of cases in the specified previous medical history category
n (%) = number (percentage) of cases in the specified category of diagnosis OR symptom category
95% CI = exact 95% confidence interval - L.L. = lower limit, U.L. = upper limit
ASD. TR = ATRIAL SEPTAL DEFECT
PUL. HTN = Pulmonary hypertension
R/O = Rule Out
AGE = Acute Gastroenteritis
GER = Gastroesophageal reflux
GERD = Gastroesophageal reflux disease
Note: In the above table, the classification of the diagnosis or sign symptoms to the respective previous medical history categories is presented as classified by the investigator.

4.4 Pre-rotavirus vaccination history

Table 5 presents the pre-rotavirus (RV) vaccination history.

- A total of 66 subjects (24 (5.5%) males and 42 (9.6%) females) received a dose of Rotarix™ prior to the start of this PMS study.

Table 5 Pre-rotavirus vaccination history (Total Vaccinated cohort)

		HRV Group			
		Female N = 436		Male N = 440	
Characteristics	Parameters or Categories	n	%	n	%
Did the subject receive HRV vaccine prior to the PMS study?	Yes	42	9.6	24	5.5
	No	394	90.4	416	94.5

HRV = Human rotavirus vaccine
N = total number of subjects
n = number of subjects with the specified category.
% = n / Number of subjects with available results x 100
YES = Subjects with a dose of HRV vaccination prior to the start of the study
No = Subject who did not received any dose of HRV vaccination prior to the start of the PMS.

4.5 Drug administration

4.5.1 Administration of concomitant medication

Table 6 presents the administration of concomitant medication by gender for the Total Vaccinated cohort.

Table 7 presents the administration of concomitant medication by classification for the Total Vaccinated cohort.

- The percentage of subjects who started taking any concomitant medication during the study period was 42.7%. Of these 12.9% received any antibiotic medication.

- Prophylactic antipyretics were taken by 1.3% of the subjects.

Table 6 Administration of concomitant medication - by gender (Total Vaccinated cohort)

			Male N=440		Female N=436		Total N =876	
	Group	Category	n	%	n	%	n	%
Administration of concomitant medication	HRV	NO	238	54.1	264	60.6	502	57.3
		YES	202	45.9	172	39.4	374	42.7

HRV = Human rotavirus vaccine
N = Total number of subjects in each group (MALE /FEMALE)
n(%) = number (percentage)of subjects with the specified category (YES / NO)

Table 7 Administration of concomitant medication - by classification (Total Vaccinated cohort)

	Group					95% CI	
		Classification	N	n	%	LL	UL
Administration of concomitant medication	HRV	Any	876	374	42.7	39.4	46.0
		Any antipyretic	876	103	11.8	9.7	14.1
		Any antibiotic	876	113	12.9	10.8	15.3
		Prophylactic antipyretic	876	11	1.3	0.6	2.2

HRV = Human rotavirus vaccine
N = Number of subjects
n (%) = number (percentage) of subjects with the specified Classification
95% CI = exact 95% confidence interval - L.L. = lower limit, U.L. = upper limit

4.5.2 Administration of concomitant vaccination

Table 8 presents the administration of concomitant vaccination by gender for the Total Vaccinated cohort.

- Overall at least 97.9% of the subjects received any concomitant vaccination with Rotarix™.

Table 8 Administration of concomitant vaccination – by gender (Total Vaccinated cohort)

Concomitant vaccination	Male N=440				Female N=436				Total N =876			
	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
Yes	430	97.7	95.9	98.9	428	98.2	96.4	99.2	858	97.9	96.8	98.8
No	10	2.3	1.1	4.1	8	1.8	0.8	3.6	18	2.1	1.2	3.2

N = Total number of subjects
n(%) = Number(percentage) of subjects with specified category

4.5.3 Administration of study vaccination

Table 9 presents the administration of study vaccine for the Total Vaccinated cohort.

- Overall, 92.5% and 79.8% of the subjects received Dose 1 and Dose 2 of Rotarix™, respectively during the study period.

- The percentage of subjects who received Dose 1 of Rotarix™ prior to the start of this study was 7.5%.

Table 9 Administration of study vaccine (Total Vaccinated cohort)

			HRV Group	
Gender	**Characteristics**	**Parameters or Categories**	**n**	**%**
Female (N=436)	Dose 1 in this study	NO	42	9.6
		YES	394	90.4
	Dose 2 in this study	NO	84	19.3
		YES	352	80.7
	Dose 1 prior to this study	NO	394	90.4
		YES	42	9.6
Male (N=440)	Dose 1 in this study	NO	24	5.5
		YES	416	94.5
	Dose 2 in this study	NO	93	21.1
		YES	347	78.9
	Dose 1 prior to this study	NO	416	94.5
		YES	24	5.5
Total (N=876)	Dose 1 in this study	NO	66	7.5
		YES	810	92.5
	Dose 2 in this study	NO	177	20.2
		YES	699	79.8
	Dose 1 prior to this study	NO	810	92.5
		YES	66	7.5

HRV = Human rotavirus vaccine
N = Total number of subjects in each group (Male/Female/Total)
n(%)= Number(percentage) of subjects with specified category(YES/NO)

V. Results of the drug use investigation

5. Results of the drug use investigation

5.1 Adverse events

In this study, there was a active collection of few adverse events (AEs) (cough, diarrhoea, irritability, loss of appetite, temperature and vomiting) for 8 days post each dose of Rotarix™ & the remaining were passively collected from the subjects for 31 days post each dose. Later all AEs were classified as expected & unexpected using the approved Korean prescribing information and the analysis was performed.

An adverse drug reaction (ADR) is any AE whose causality to the drug cannot be ruled out and is assessed as “definitely related” or “probably related” or “possibly related” or “unknown”.

Expected AEs - The presence/occurrence/intensity of an AE that is expected from the subject or an observer during the post-vaccination follow-up period as described in the approved prescribing information.

Unexpected AEs - Any AE that are not reflected in the approved prescribing information and that has been reported.

5.1.1 Serious adverse events, adverse drug reaction

Serious Adverse Event

A serious adverse event (SAE) was any untoward medical occurrence that:

a. resulted in death,

b. was life-threatening,

NOTE: The term 'life-threatening' in the definition of 'serious' referred to an event in which the subject was at risk of death at the time of the event. It did not refer to an event, which hypothetically might have caused death, if it were more severe.

c. required hospitalisation or prolongation of existing hospitalisation,

NOTE: In general, hospitalisation signified that the subject was detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician’s office or out-patient setting. Complications that occurred during hospitalisation were AEs. If a complication prolonged hospitalisation or fulfilled any other serious criteria, the event was serious. When in doubt as to whether “hospitalisation” occurred or was necessary, the AE was considered serious.

Hospitalisation for elective treatment of a pre-existing condition that did not worsen from baseline was not considered an AE.

d. resulted in disability/incapacity, or

NOTE: The term disability meant a substantial disruption of a person’s ability to conduct normal life functions. This definition was not intended to include experiences of

relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhoea, influenza, and accidental trauma (e.g. sprained ankle) which may have interfered or prevented everyday life functions but did not constitute a substantial disruption.

e. was a congenital anomaly/birth defect in the offspring of a study subject.

Medical or scientific judgement was exercised in deciding whether reporting was appropriate in other situations, such as important medical events that may not have been immediately life-threatening or resulted in death or hospitalisation but may have jeopardised the subject or may have required medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These were also considered serious. Examples of such events were invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalisation.

Table 10 presents the serious adverse events (SAEs) and serious adverse drug reactions (ADRs) for the Total Vaccinated cohort.

Table 11 presents the listings of SAEs for the Total Vaccinated cohort.

A total of 11 SAEs were reported for 6 subjects during the study period. No serious ADRs were reported during the study period.

A brief summary of these SAEs are given below.

- **Case ID:** PPD An eleven-week old male subject (subject No. PPD developed sepsis 11 days after receiving Dose 1 of Rotarix™. The subject was hospitalised and treated with antibiotics and fluid therapy. The event resolved after 23 days. The investigator concluded that the SAE was probably not related to the study vaccination.

- **Case ID:** PPD A nine-week old male subject (subject No. PPD developed bronchiolitis, otitis media acute and acute GE one day after receiving Dose 1 of Rotarix™. The subject was hospitalised and treated with Zaditen and Codenal. The event resolved after 34 days. The investigator concluded that the SAEs were probably not related to the study vaccination.

- **Case ID:** PPD An eleven-week old male subject (subject No. PPD developed acute bronchiolitis, 7 days after receiving Dose 1 of Rotarix™. The subject was hospitalised and treated with nebulizer and mucolytic agent. The event resolved after 14 days. The investigator concluded that the SAE was probably not related to the study vaccination.

- **Case ID:** PPD An eight-week old female subject (subject No. PPD developed acute GE and paralytic ileus, on the day of vaccination after receiving Dose 1 of Rotarix™. The subject was hospitalised and treated with antibiotics and fluid therapy. The event resolved after 22 days. The investigator concluded that the SAEs were probably not related to the study vaccination.

- **Case ID:** PPD A ten-week old female subject (subject No. PPD developed acute bronchiolitis, 17 days after receiving Dose 1 of Rotarix™. The subject was

hospitalised and treated with nebulizer and IV injection. The event resolved after 34 days. The investigator concluded that the SAE was probably not related to the study vaccination.

- **Case ID:** PPD A fourteen-week old male subject (subject No. PPD developed acute bronchiolitis, 45 days after receiving Dose 1 of Rotarix™. The subject was hospitalised and treated with nebulizer, antibiotics and fluid therapy. The event resolved after 8 days. The investigator concluded that the SAE was probably not related to the study vaccination.

- **Case ID:** PPD A seventeen-week old male subject (subject No. PPD developed infectious croup, 10 days after receiving Dose 2 of Rotarix™. The subject was hospitalised and treated with nebulizer, antibiotics and fluid therapy. The event resolved after 9 days. The investigator concluded the SAE was not probably related to the study vaccination.

- **Case ID:** PPD A seventeen-week old male subject (subject No. PPD developed AOM, 10 days after receiving Dose 2 of Rotarix™. The subject was hospitalised and treated with nebulizer, antibiotics and fluid therapy. The event resolved after 9 days. The investigator concluded that the SAE was not probably related to the study vaccination.

Table 10 Serious adverse events and serious adverse drug reactions (Total Vaccinated cohort)

		SAE N=876					ADR N=876				
					95%					95%	
System organ class (code)	Prefered Term	n	n*	%	LL	UL	n	n*	%	LL	UL
Gastrointestinal disorders (10017947)	Ileus paralytic (10021333)	1	1	0.1	0.0	0.6	.	.		.	.
Infections and infestations (10021881)	Bronchiolitis (10006448)	4	4	0.5	0.1	1.2	.	.		.	.
	Croup infectious (10011416)	1	1	0.1	0.0	0.6	.	.		.	.
	Gastroenteritis (10017888)	2	2	0.2	0.0	0.8	.	.		.	.
	Otitis media acute (10033079)	2	2	0.2	0.0	0.8	.	.		.	.
	Sepsis (10040047)	1	1	0.1	0.0	0.6	.	.		.	.

N = Number of subjects
n (%) = number (percentage) of subjects with the specified category
n* = number of symptoms with the specified category
95% CI = exact 95% confidence interval - L.L. = lower limit, U.L. = upper limit

Table 11 Listing of SAEs (Total Vaccinated cohort)

Group	Sub. No.	Case Id	Age at onset (Week)	Gender	Verbatim	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Intensity	Causality**	Outcome
HRV	PPD		11	M	1. r/o sepsis, 2. fever, 3. iv antibiotics and fluid therapy	Sepsis	Infections and infestations	HO	1	11	23	1	N	Recovered/resolved
			9	M	Note*	Bronchiolitis	Infections and infestations	HO	1	1	34	3	N	Recovered/resolved
			9		Note*	Gastroenteritis	Infections and infestations	HO	1	1	34	3	N	Recovered/resolved
			9		Note*	Otitis media acute	Infections and infestations	HO	1	1	34	3	N	Recovered/resolved
			11	M	Acute bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	7	14	2	N	Recovered/resolved
			8	F	Acute gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	0	22	2	N	Recovered/resolved
			8		Paralytic ileus	Ileus paralytic	Gastrointestinal disorders	HO	1	0	22	2	N	Recovered/resolved
			10	F	Acute bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	17	34	2	N	Recovered/resolved
			14	M	Acute bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	45	8	2	N	Recovered/resolved
			17	M	Croup, acute otitis media	Croup infectious	Infections and infestations	HO	2	10	9	2	N	Recovered/resolved
			17		Croup, acute otitis media	Otitis media acute	Infections and infestations	HO	2	10	9	2	N	Recovered/resolved

HRV = Human rotavirus vaccine
M = Male
F = Female
MA type (Medical Advice type): HO: Hospitalisation
* Bronchiolitis, otitis media acute and acute GE.
** Causality according to KFDA assessment = probably not related to the Rotarix™ vaccine

5.1.2 Adverse events, adverse drug reaction

Table 12 presents the expected and unexpected AEs and ADRs for the Total Vaccinated cohort.

- Irritability was the most frequently reported expected AE, reported for 405 (46.2%) subjects. Decreased appetite and vomiting were reported for 259 (29.6%) and 200 (22.8%) subjects, respectively.

- Irritability was the most frequently reported expected ADR, reported for 47 (5.4%) subjects. Vomiting and pyrexia were reported for 44 (5.0%) and 27 (3.1%) subjects, respectively.

- Cough was the most frequently reported unexpected AE, reported for 209 (23.9%) subjects. Nasopharyngitis (79 (9.0%) subjects), bronchiolitis (64 (7.3%) subjects), dermatitis atopic (34 (3.9%) subjects) and gastrointestinal disorders (26 (3.0%) subjects) were the other reported unexpected AEs.

- Cough was also the most frequently reported unexpected ADR reported for (10 (1.1%)) subjects. Upper respiratory tract infection and gastrointestinal disorders were reported for 5 (0.6%) subjects and 3 (0.3%) subjects, respectively.

Table 12 Expected & Unexpected adverse events and adverse drug reactions (Total Vaccinated cohort)

			AE N=876					ADR N=876				
						95%					95%	
Group	System organ class (code)	Preferred Term (code)	n	n*	%	LL	UL	n	n*	%	LL	UL
Expected Adverse Events*												
HRV	Gastrointestinal disorders (10017947)	Constipation (10010774)	5	5	0.6	0.2	1.3	.	.		.	.
		Diarrhoea (10012735)	55	56	6.3	4.8	8.1	15	16	1.7	1.0	2.8
		Vomiting (10047700)	200	224	22.8	20.1	25.8	44	45	5.0	3.7	6.7
	General disorders and administration site conditions (10018065)	Irritability (10022998)	405	488	46.2	42.9	49.6	47	53	5.4	4.0	7.1
		Pyrexia (10037660)	138	150	15.8	13.4	18.3	27	29	3.1	2.0	4.5
	Infections and infestations (10021881)	Upper respiratory tract infection (10046306)	57	65	6.5	5.0	8.3	.	.		.	.
	Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	259	296	29.6	26.6	32.7	26	26	3.0	1.9	4.3
	Respiratory, thoracic and mediastinal disorders (10038738)	Rhinorrhoea (10039101)	6	6	0.7	0.3	1.5	.	.		.	.
	Skin and subcutaneous tissue disorders (10040785)	Dermatitis (10012431)	12	12	1.4	0.7	2.4	.	.		.	.
		Rash (10037844)	2	2	0.2	0.0	0.8	.	.		.	.
Unexpected Adverse events*												
HRV	Eye disorders (10015919)	Conjunctivitis (10010741)	7	7	0.8	0.3	1.6	.	.		.	.
		Conjunctivitis allergic (10010744)	1	1	0.1	0.0	0.6	.	.		.	.
		Entropion (10061842)	1	1	0.1	0.0	0.6	.	.		.	.
		Eye discharge (10015915)	2	2	0.2	0.0	0.8	.	.		.	.
	Gastrointestinal disorders (10017947)	Colitis (10009887)	2	2	0.2	0.0	0.8	.	.		.	.
		Dyspepsia (10013946)	3	3	0.3	0.1	1.0	.	.		.	.
		Gastritis (10017853)	8	10	0.9	0.4	1.8	.	.		.	.
		Gastrointestinal disorder (10017944)	26	27	3.0	1.9	4.3	3	3	0.3	0.1	1.0
		Gastrooesophageal reflux disease (10017885)	2	2	0.2	0.0	0.8	.	.		.	.
		Ileus paralytic (10021333)	1	1	0.1	0.0	0.6	.	.		.	.
		Regurgitation (10067171)	1	1	0.1	0.0	0.6	.	.		.	.
	General disorders and	Ulcer (10045285)	1	1	0.1	0.0	0.6	.	.		.	.

			AE N=876					ADR N=876				
						95%					95%	
Group	System organ class (code)	Preferred Term (code)	n	n*	%	LL	UL	n	n*	%	LL	UL
	administration site conditions (10018065)											
	Immune system disorders (10021428)	Atopy (10003645)	6	6	0.7	0.3	1.5	.	.		.	.
		Hypersensitivity (10020751)	2	2	0.2	0.0	0.8	1	1	0.1	0.0	0.6
		Milk allergy (10027633)	1	1	0.1	0.0	0.6	.	.		.	.
	Infections and infestations (10021881)	Acute sinusitis (10001076)	3	3	0.3	0.1	1.0	.	.		.	.
		Acute tonsillitis (10001093)	4	4	0.5	0.1	1.2	.	.		.	.
		Bronchiolitis (10006448)	64	78	7.3	5.7	9.2	2	2	0.2	0.0	0.8
		Bronchitis (10006451)	12	12	1.4	0.7	2.4	.	.		.	.
		Cellulitis (10007882)	2	2	0.2	0.0	0.8	.	.		.	.
		Croup infectious (10011416)	1	1	0.1	0.0	0.6	.	.		.	.
		Cystitis (10011781)	1	1	0.1	0.0	0.6	.	.		.	.
		Ear infection (10014011)	1	1	0.1	0.0	0.6	.	.		.	.
		Empyema (10014568)	3	3	0.3	0.1	1.0	.	.		.	.
		Enteritis infectious (10058839)	1	1	0.1	0.0	0.6	.	.		.	.
		Fungal infection (10017533)	1	1	0.1	0.0	0.6	.	.		.	.
		Gastroenteritis (10017888)	24	29	2.7	1.8	4.0	1	1	0.1	0.0	0.6
		Gastroenteritis viral (10017918)	2	2	0.2	0.0	0.8	.	.		.	.
		Influenza (10022000)	1	1	0.1	0.0	0.6	.	.		.	.
		Laryngitis (10023874)	1	1	0.1	0.0	0.6	.	.		.	.
		Lower respiratory tract infection (10024968)	2	3	0.2	0.0	0.8	.	.		.	.
		Nasopharyngitis (10028810)	79	99	9.0	7.2	11.1	.	.		.	.
		Oral candidiasis (10030963)	4	5	0.5	0.1	1.2	.	.		.	.
		Otitis externa (10033072)	2	2	0.2	0.0	0.8	.	.		.	.
		Otitis media (10033078)	7	7	0.8	0.3	1.6	1	1	0.1	0.0	0.6
		Otitis media acute (10033079)	7	8	0.8	0.3	1.6	.	.		.	.
		Pharyngitis (10034835)	10	13	1.1	0.5	2.1	.	.		.	.

			AE N=876					ADR N=876				
						95%					95%	
Group	System organ class (code)	Preferred Term (code)	n	n*	%	LL	UL	n	n*	%	LL	UL
		Pneumonia (10035664)	3	3	0.3	0.1	1.0	.	.		.	.
		Respiratory tract infection (10062352)	2	4	0.2	0.0	0.8	.	.		.	.
		Rhinitis (10039083)	8	12	0.9	0.4	1.8	.	.		.	.
		Sepsis (10040047)	1	1	0.1	0.0	0.6	.	.		.	.
		Tonsillitis (10044008)	1	2	0.1	0.0	0.6	.	.		.	.
		Upper respiratory tract infection (10046306)	24	25	2.7	1.8	4.0	5	5	0.6	0.2	1.3
		Urethritis (10046480)	1	1	0.1	0.0	0.6	.	.		.	.
		Urinary tract infection (10046571)	1	1	0.1	0.0	0.6	.	.		.	.
	Nervous system disorders (10029205)	Tremor (10044565)	1	1	0.1	0.0	0.6	.	.		.	.
	Pregnancy, puerperium and perinatal conditions (10036585)	Jaundice neonatal (10023138)	1	1	0.1	0.0	0.6	.	.		.	.
	Renal and urinary disorders (10038359)	Tubulointerstitial nephritis (10048302)	1	1	0.1	0.0	0.6	.	.		.	.
	Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	1	1	0.1	0.0	0.6	.	.		.	.
	Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	2	2	0.2	0.0	0.8	.	.		.	.
		Cough (10011224)	209	243	23.9	21.1	26.8	10	11	1.1	0.5	2.1
		Nasal congestion (10028735)	3	3	0.3	0.1	1.0	.	.		.	.
		Rhinorrhoea (10039101)	1	1	0.1	0.0	0.6	.	.		.	.
	Skin and subcutaneous tissue disorders (10040785)	Dermatitis atopic (10012438)	34	37	3.9	2.7	5.4	1	1	0.1	0.0	0.6
		Dermatitis contact (10012442)	2	2	0.2	0.0	0.8	.	.		.	.
		Dermatitis diaper (10012444)	6	6	0.7	0.3	1.5	.	.		.	.
		Eczema (10014184)	2	2	0.2	0.0	0.8	.	.		.	.
		Rash (10037844)	1	1	0.1	0.0	0.6	.	.		.	.
		Seborrhoeic dermatitis (10039793)	4	5	0.5	0.1	1.2	.	.		.	.
		Skin lesion (10040882)	1	1	0.1	0.0	0.6	.	.		.	.
		Urticaria (10046735)	4	4	0.5	0.1	1.2	1	1	0.1	0.0	0.6

HRV = Human rotavirus vaccine
N = Number of subjects
n(%) = number (percentage) of subjects with the specified category
n* = number of symptoms with the specified category
95% CI = exact 95% confidence interval - L.L. = lower limit, U.L. = upper limit
* The classification of adverse events as Expected & Unexpected AEs is done by Low level term code mentioned in the cleaning report of this study

5.1.3 Adverse events by factors

A. Adverse events by patient background factors

A.1 Gender

Table 13 presents the AEs experienced by subjects during the entire study period: Stratified by gender for the Total Vaccinated cohort.

The percentage of male (72.5%) and female (71.3%) subjects reporting AEs were similar during the study period.

Table 13 Adverse events experienced by subjects during the entire study period: Stratified by gender (Total Vaccinated cohort)

		MALE N = 440				FEMALE N = 436			
				95% CI				95% CI	
Group	Did the subject experience any adverse events?	n	%	LL	UL	n	%	LL	UL
HRV	No	121	27.5	23.4	31.9	125	28.7	24.5	33.2
	Yes	319	72.5	68.1	76.6	311	71.3	66.8	75.5

HRV = Human rotavirus vaccine
N = Total number of subjects in the given category
n(%) = number(percentage)of subjects in the given category

A.2 Age

Not applicable.

A.3 Medical history

Table 14 presents the AEs experienced by subjects during the entire study period: stratified by previous medical history for the Total Vaccinated cohort.

Table 15 presents the AEs experienced by previous medical history-by gender and classification for the Total Vaccinated cohort.

- Of the 118 subjects who had a previous medical history a total of 85 (72.0%) subjects experienced AEs.

- Irritability was the most frequently reported AE among subjects who had a previous medical history of blood and lymphatic system (4 subjects), eye disorders (10

subjects), GI disorders (17 subjects), hepatobiliary disorders (8 subjects), metabolism and nutrition disorders (3 subjects), respiratory, thoracic and mediastinal disorders (26 subjects), skin and subcutaneous tissue disorders (13 subjects) and subjects who had other AEs (5 subjects)

- Cough, irritability, decreased appetite and nasopharyngitis were the reported AEs among subjects who had a previous medical history of cardiac disorders and were reported for two subjects each.

- Cough, irritability and vomiting were the most frequently reported AEs among subjects who had a previous medical history of ear and labyrinth disorders and was reported for three subjects each.

- Cough and irritability were reported for 1 subject each among subjects who had a previous medical history of endocrine disorders and infections and infestations each.

- Irritability, pyrexia and vomiting were reported for 1 subject each among subjects who had a previous medical history of neoplasms benign, malignant and unspecified (including cysts and polyps).

- None of the subjects who had a previous medical history of immune system disorders reported any AE.

Table 14 Adverse events experienced by subjects during the entire study period: Stratified by previous medical history (Total Vaccinated cohort)

		Did the subject have any previous medical history?							
		YES N=118				NO N=758			
				95% CI				95% CI	
Group	Did the subject experience any adverse event?	n	%	LL	UL	n	%	LL	UL
HRV	No	33	28.0	20.1	37.0	213	28.1	24.9	31.4
	Yes	85	72.0	63.0	79.9	545	71.9	68.6	75.1

HRV = Human rotavirus vaccine
N = Total number of subjects in the given category
n(%) = number(percentage) of subjects in the given category

Table 15 Adverse events experienced by medical history - by gender and classification (Total Vaccinated cohort)

		Male N=440				Female N=436				Total N=876			
				95% CI				95% CI				95% CI	
Previous Medical history	Preferred Term (code)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
BLOOD AND LYMPHATIC SYSTEM	Bronchitis (10006451)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Decreased appetite (10061428)	1	0.2	0.0	1.3	2	0.5	0.1	1.6	3	0.3	0.1	1.0
	Irritability (10022998)	2	0.5	0.1	1.6	2	0.5	0.1	1.6	4	0.5	0.1	1.2
	NO SYMPTOM	0	0.0	0.0	0.8	3	0.7	0.1	2.0	3	0.3	0.1	1.0
	Vomiting (10047700)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
CARDIAC	Cough (10011224)	1	0.2	0.0	1.3	1	0.2	0.0	1.3	2	0.2	0.0	0.8
	Decreased appetite (10061428)	1	0.2	0.0	1.3	1	0.2	0.0	1.3	2	0.2	0.0	0.8
	Irritability (10022998)	1	0.2	0.0	1.3	1	0.2	0.0	1.3	2	0.2	0.0	0.8
	Nasopharyngitis (10028810)	1	0.2	0.0	1.3	1	0.2	0.0	1.3	2	0.2	0.0	0.8
	Pyrexia (10037660)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Vomiting (10047700)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
EAR AND LABYRINTH	Cough (10011224)	3	0.7	0.1	2.0	0	0.0	0.0	0.8	3	0.3	0.1	1.0
	Decreased appetite (10061428)	2	0.5	0.1	1.6	0	0.0	0.0	0.8	2	0.2	0.0	0.8
	Irritability (10022998)	3	0.7	0.1	2.0	0	0.0	0.0	0.8	3	0.3	0.1	1.0
	Pyrexia (10037660)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Seborrhoeic dermatitis (10039793)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Vomiting (10047700)	2	0.5	0.1	1.6	1	0.2	0.0	1.3	3	0.3	0.1	1.0
ENDOCRINE	Cough (10011224)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Irritability (10022998)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
EYE	Cough (10011224)	2	0.5	0.1	1.6	3	0.7	0.1	2.0	5	0.6	0.2	1.3
	Decreased appetite (10061428)	0	0.0	0.0	0.8	4	0.9	0.3	2.3	4	0.5	0.1	1.2
	Diarrhoea (10012735)	2	0.5	0.1	1.6	0	0.0	0.0	0.8	2	0.2	0.0	0.8
	Eye discharge (10015915)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6

		Male N=440				Female N=436				Total N=876			
				95% CI				95% CI				95% CI	
Previous Medical history	**Preferred Term (code)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Irritability (10022998)	6	1.4	0.5	2.9	4	0.9	0.3	2.3	10	1.1	0.5	2.1
	NO SYMPTOM	1	0.2	0.0	1.3	2	0.5	0.1	1.6	3	0.3	0.1	1.0
	Pyrexia (10037660)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Seborrhoeic dermatitis (10039793)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Upper respiratory tract infection (10046306)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Vomiting (10047700)	1	0.2	0.0	1.3	2	0.5	0.1	1.6	3	0.3	0.1	1.0
GASTROINTESTINAL	Cough (10011224)	2	0.5	0.1	1.6	3	0.7	0.1	2.0	5	0.6	0.2	1.3
	Decreased appetite (10061428)	6	1.4	0.5	2.9	6	1.4	0.5	3.0	12	1.4	0.7	2.4
	Dermatitis atopic (10012438)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Diarrhoea (10012735)	2	0.5	0.1	1.6	0	0.0	0.0	0.8	2	0.2	0.0	0.8
	Gastritis (10017853)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Gastroenteritis (10017888)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Gastrointestinal disorder (10017944)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Irritability (10022998)	11	2.5	1.3	4.4	6	1.4	0.5	3.0	17	1.9	1.1	3.1
	NO SYMPTOM	5	1.1	0.4	2.6	6	1.4	0.5	3.0	11	1.3	0.6	2.2
	Nasopharyngitis (10028810)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Otitis media acute (10033079)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Pyrexia (10037660)	7	1.6	0.6	3.3	3	0.7	0.1	2.0	10	1.1	0.5	2.1
	Regurgitation (10067171)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Rhinorrhoea (10039101)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Seborrhoeic dermatitis (10039793)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Upper respiratory tract infection (10046306)	0	0.0	0.0	0.8	2	0.5	0.1	1.6	2	0.2	0.0	0.8
	Vomiting (10047700)	6	1.4	0.5	2.9	2	0.5	0.1	1.6	8	0.9	0.4	1.8
HEPATOBILIARY	Cough (10011224)	1	0.2	0.0	1.3	1	0.2	0.0	1.3	2	0.2	0.0	0.8
	Decreased appetite	0	0.0	0.0	0.8	4	0.9	0.3	2.3	4	0.5	0.1	1.2

		Male N=440				Female N=436				Total N=876			
				95% CI				95% CI				95% CI	
Previous Medical history	Preferred Term (code)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	(10061428)												
	Diarrhoea (10012735)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Irritability (10022998)	4	0.9	0.2	2.3	4	0.9	0.3	2.3	8	0.9	0.4	1.8
	NO SYMPTOM	1	0.2	0.0	1.3	1	0.2	0.0	1.3	2	0.2	0.0	0.8
	Nasopharyngitis (10028810)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Pyrexia (10037660)	3	0.7	0.1	2.0	1	0.2	0.0	1.3	4	0.5	0.1	1.2
	Upper respiratory tract infection (10046306)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Vomiting (10047700)	3	0.7	0.1	2.0	3	0.7	0.1	2.0	6	0.7	0.3	1.5
IMMUNE SYSTEM (INCL ALLERGIES, AUTOIMMUNE DISORDERS)	NO SYMPTOM	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
INFECTIONS AND INFESTATIONS	Cough (10011224)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Irritability (10022998)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
METABOLISM AND NUTRITION	Decreased appetite (10061428)	1	0.2	0.0	1.3	1	0.2	0.0	1.3	2	0.2	0.0	0.8
	Irritability (10022998)	2	0.5	0.1	1.6	1	0.2	0.0	1.3	3	0.3	0.1	1.0
	Pyrexia (10037660)	2	0.5	0.1	1.6	0	0.0	0.0	0.8	2	0.2	0.0	0.8
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS, POLYPS)	Irritability (10022998)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Pyrexia (10037660)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Vomiting (10047700)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
OTHER	Cellulitis (10007882)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Cough (10011224)	1	0.2	0.0	1.3	2	0.5	0.1	1.6	3	0.3	0.1	1.0
	Decreased appetite (10061428)	1	0.2	0.0	1.3	2	0.5	0.1	1.6	3	0.3	0.1	1.0
	Diarrhoea (10012735)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Dyspepsia (10013946)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Gastroenteritis (10017888)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Gastrointestinal disorder (10017944)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6

		Male N=440				Female N=436				Total N=876			
				95% CI				95% CI				95% CI	
Previous Medical history	**Preferred Term (code)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Irritability (10022998)	2	0.5	0.1	1.6	3	0.7	0.1	2.0	5	0.6	0.2	1.3
	NO SYMPTOM	1	0.2	0.0	1.3	4	0.9	0.3	2.3	5	0.6	0.2	1.3
	Nasopharyngitis (10028810)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Pyrexia (10037660)	1	0.2	0.0	1.3	2	0.5	0.1	1.6	3	0.3	0.1	1.0
	Vomiting (10047700)	0	0.0	0.0	0.8	2	0.5	0.1	1.6	2	0.2	0.0	0.8
RESPIRATORY, THORACIC AND MEDIASTINAL	Acute sinusitis (10001076)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Bronchiolitis (10006448)	2	0.5	0.1	1.6	0	0.0	0.0	0.8	2	0.2	0.0	0.8
	Bronchitis (10006451)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Cough (10011224)	9	2.0	0.9	3.8	6	1.4	0.5	3.0	15	1.7	1.0	2.8
	Decreased appetite (10061428)	9	2.0	0.9	3.8	8	1.8	0.8	3.6	17	1.9	1.1	3.1
	Dermatitis (10012431)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Diarrhoea (10012735)	4	0.9	0.2	2.3	2	0.5	0.1	1.6	6	0.7	0.3	1.5
	Gastroenteritis (10017888)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Irritability (10022998)	16	3.6	2.1	5.8	10	2.3	1.1	4.2	26	3.0	1.9	4.3
	NO SYMPTOM	4	0.9	0.2	2.3	4	0.9	0.3	2.3	8	0.9	0.4	1.8
	Nasal congestion (10028735)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Nasopharyngitis (10028810)	0	0.0	0.0	0.8	3	0.7	0.1	2.0	3	0.3	0.1	1.0
	Oral candidiasis (10030963)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Otitis media acute (10033079)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Pyrexia (10037660)	7	1.6	0.6	3.3	4	0.9	0.3	2.3	11	1.3	0.6	2.2
	Regurgitation (10067171)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Rhinorrhoea (10039101)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Seborrhoeic dermatitis (10039793)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Upper respiratory tract infection (10046306)	0	0.0	0.0	0.8	6	1.4	0.5	3.0	6	0.7	0.3	1.5
	Vomiting (10047700)	8	1.8	0.8	3.6	6	1.4	0.5	3.0	14	1.6	0.9	2.7
SKIN AND	Bronchiolitis	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6

		Male N=440				Female N=436				Total N=876			
				95% CI				95% CI				95% CI	
Previous Medical history	**Preferred Term (code)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
SUBCUTANEOUS TISSUE	(10006448)												
	Cough (10011224)	3	0.7	0.1	2.0	2	0.5	0.1	1.6	5	0.6	0.2	1.3
	Decreased appetite (10061428)	4	0.9	0.2	2.3	3	0.7	0.1	2.0	7	0.8	0.3	1.6
	Dermatitis (10012431)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Dermatitis atopic (10012438)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Diarrhoea (10012735)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Irritability (10022998)	9	2.0	0.9	3.8	4	0.9	0.3	2.3	13	1.5	0.8	2.5
	NO SYMPTOM	5	1.1	0.4	2.6	3	0.7	0.1	2.0	8	0.9	0.4	1.8
	Nasopharyngitis (10028810)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Otitis externa (10033072)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Otitis media acute (10033079)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Pyrexia (10037660)	3	0.7	0.1	2.0	2	0.5	0.1	1.6	5	0.6	0.2	1.3
	Regurgitation (10067171)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Rhinorrhoea (10039101)	1	0.2	0.0	1.3	0	0.0	0.0	0.8	1	0.1	0.0	0.6
	Upper respiratory tract infection (10046306)	0	0.0	0.0	0.8	1	0.2	0.0	1.3	1	0.1	0.0	0.6
	Vomiting (10047700)	8	1.8	0.8	3.6	1	0.2	0.0	1.3	9	1.0	0.5	1.9

N = Total number of subjects in the given category
n (%) = number (percentage)of subjects in the given category
NO SYMPTOM = Subjects who had the corresponding previous medical history, but didn't report **any AE.**

A.4 Concomitant medications

Table 16 presents the AEs experienced by subjects during the entire study period: stratified by medication for the Total Vaccinated cohort.

Table 17 presents AEs experienced by subjects - by classification of concomitant medication for the Total Vaccinated cohort.

- Majority (96.5%) of the subjects who experienced an AE during the study period took any medication.
- The percentage of subjects who took any concomitant medication to treat an AE was 89.3%.
- The percentage of subjects who took any antibiotics to treat an AE was 93.8%.
- Of the 11 subjects who took prophylactic antipyretics 90.9% of the subjects reported an AE.

Table 16 Adverse events experienced by subjects during the entire study period : Stratified by medication (Total Vaccinated cohort)

		Did the subject receive any medication?							
		YES N = 374				NO N = 502			
				95% CI				95% CI	
Group	Did the subject experience any adverse events?	n	%	LL	UL	n	%	LL	UL
HRV	No	13	3.5	1.9	5.9	233	46.4	42.0	50.9
	Yes	361	96.5	94.1	98.1	269	53.6	49.1	58.0

HRV = Human rotavirus vaccine
N = Total number of subjects in the given category
n(%) = number(percentage)of subjects in the given category

Table 17 Adverse events experienced by subjects - by classification of concomitant medication (Total Vaccinated cohort)

				Adverse events							
				Yes				No			
						95% CI				95% CI	
Group	Classification	Is drug used for treating an AE?	N	n	%	LL	UL	n	%	LL	UL
HRV	Any Medication	No	374	27	7.2	4.8	10.3	13	3.5	1.9	5.9
		Yes	374	334	89.3	85.7	92.2	.	0.0	.	1.0
	Any antibiotics	No	113	6	5.3	2.0	11.2	1	0.9	0.0	4.8
		Yes	113	106	93.8	87.7	97.5	.	0.0	.	3.2
	Any antipyretic	No	103	12	11.7	6.2	19.5	6	5.8	2.2	12.2
		Yes	103	85	82.5	73.8	89.3	.	0.0	.	3.5
	Phrophylactic Antipyretics	No	11	10	90.9	58.7	99.8	1	9.1	0.2	41.3

HRV = Human rotavirus vaccine
N = Total number of subjects in the given classification
n(%) = number(percentage)of subjects in the given classification

A.5 Concomitant vaccinations

Table 18 presents the AEs experienced by subjects during the entire study period: stratified by concomitant vaccination for the Total Vaccinated cohort.

Table 19 presents the AEs experienced by subjects - by classification of concomitant vaccination for the Total Vaccinated cohort.

- Of the 858 subjects who received any paediatric vaccination other than Rotarix™ in this study 620 (72.3%) subjects reported an AE.
- Of the 815 subjects who received *Haemophilus influenza* type b (Hib) vaccine in this study 598 (73.4%) subjects reported an AE.
- Of the 776 subjects who received pneumococcal (Pn) vaccine in this study 570 (73.5%) subjects reported an AE.
- Of the 465 subjects who received the diphtheria-tetanus-pertussis (DTP) vaccine in this study 336 (72.3%) subjects reported an AE.

Table 18 Adverse events experienced by subjects during the entire study period: Stratified by concomitant vaccination (Total Vaccinated cohort)

		Did the subject receive any concomitant vaccination?							
		YES N = 858				NO N = 18			
				95% CI				95% CI	
Group	Did the subject experience any adverse event?	n	%	LL	UL	n	%	LL	UL
HRV	No	238	27.7	24.8	30.9	8	44.4	21.5	69.2
	Yes	620	72.3	69.1	75.2	10	55.6	30.8	78.5

HRV = Human rotavirus vaccine
N = Total number of subjects in the given category
n(%) = number(percentage)of subjects in the given category

Table 19 Adverse events experienced by subjects - by classification of concomitant vaccination (Total Vaccinated cohort)

			Adverse events							
			Yes				No			
					95% CI				95% CI	
Group	Classification	N	n	%	LL	UL	n	%	LL	UL
HRV	ANY	858	620	72.3	69.1	75.2	238	27.7	24.8	30.9
	BCG	29	19	65.5	45.7	82.1	10	34.5	17.9	54.3
	DTP	465	336	72.3	67.9	76.3	129	27.7	23.7	32.1
	DTPa	69	59	85.5	75.0	92.8	10	14.5	7.2	25.0
	HBV	155	122	78.7	71.4	84.9	33	21.3	15.1	28.6
	HIB	815	598	73.4	70.2	76.4	217	26.6	23.6	29.8
	IPV	456	329	72.1	67.8	76.2	127	27.9	23.8	32.2
	MeMuRu	1	1	100	2.5	100.0	0	0.0	0.0	97.5
	PCV	2	1	50.0	1.3	98.7	1	50.0	1.3	98.7
	Pn	776	570	73.5	70.2	76.5	206	26.5	23.5	29.8
	RAB	54	45	83.3	70.7	92.1	9	16.7	7.9	29.3

HRV = Human rotavirus vaccine
N = Total number of subjects in the given classification
n(%) = number(percentage)of subjects in the given classification

Table 20 presents the AEs by medical history, concomitant vaccination and concomitant medication for the Total Vaccinated cohort.

- Overall, at least one expected AE was reported for 62.7% of the subjects who had a previous medical history, 66.0% of subjects who received concomitant medication and 58.3% of the subjects who received concomitant vaccination, respectively.

- Irritability was the most frequently reported expected AE reported for 55.1% of the subjects who had previous medical history, 47.3% of subjects who received concomitant medication and 46.2% of the subjects who received concomitant vaccination, respectively.

- Overall, at least one unexpected AE was reported for 43.2% of the subjects who had a previous medical history, 82.9% of the subjects who received concomitant medication and 46.7% of subjects who received concomitant vaccination, respectively.

- Cough was the most frequently reported unexpected AE reported for 26.3% of the subjects who had previous medical history, 30.5% of the subjects who received concomitant medication and 23.9% of subjects who received concomitant vaccination, respectively.

Table 20 Expected & Unexpected adverse events by medical history, concomitant vaccination, concomitant medication (Total Vaccinated cohort)

Preferred term (code)	Medical History				Concomitant medication				Concomitant vaccination			
	Yes N=118		No N=758		Yes N=374		No N=502		Yes N=858		No N=18	
	n	%	n	%	n	%	n	%	n	%	n	%
Expected adverse events*												
Constipation (10010774)	0	0.0	5	0.7	5	1.3	0	0.0	5	0.6	0	0.0
Decreased appetite (10061428)	41	34.7	218	28.8	121	32.4	138	27.5	256	29.8	3	16.7
Dermatitis (10012431)	2	1.7	10	1.3	12	3.2	0	0.0	12	1.4	0	0.0
Diarrhoea (10012735)	10	8.5	45	5.9	35	9.4	20	4.0	54	6.3	1	5.6
Irritability (10022998)	65	55.1	340	44.9	177	47.3	228	45.4	396	46.2	9	50.0
Pyrexia (10037660)	28	23.7	110	14.5	61	16.3	77	15.3	136	15.9	2	11.1
Rash (10037844)	0	0.0	2	0.3	1	0.3	1	0.2	2	0.2	0	0.0
Rhinorrhoea (10039101)	1	0.8	5	0.7	6	1.6	0	0.0	6	0.7	0	0.0
Upper respiratory tract infection (10046306)	3	2.5	54	7.1	57	15.2	0	0.0	56	6.5	1	5.6
Vomiting (10047700)	30	25.4	170	22.4	87	23.3	113	22.5	195	22.7	5	27.8
Total	**74**	**62.7**	**436**	**57.5**	**247**	**66.0**	**263**	**52.4**	**500**	**58.3**	**10**	**55.6**
Unexpected adverse events*												
Acute sinusitis (10001076)	1	0.8	2	0.3	3	0.8	0	0.0	3	0.3	0	0.0
Acute tonsillitis (10001093)	0	0.0	4	0.5	4	1.1	0	0.0	4	0.5	0	0.0
Asthma (10003553)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Atopy (10003645)	0	0.0	6	0.8	6	1.6	0	0.0	6	0.7	0	0.0
Balanoposthitis (10004078)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Bronchiolitis (10006448)	2	1.7	62	8.2	64	17.1	0	0.0	64	7.5	0	0.0
Bronchitis (10006451)	2	1.7	10	1.3	12	3.2	0	0.0	12	1.4	0	0.0
Cellulitis (10007882)	1	0.8	1	0.1	2	0.5	0	0.0	2	0.2	0	0.0
Colitis (10009887)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Conjunctivitis (10010741)	0	0.0	7	0.9	7	1.9	0	0.0	7	0.8	0	0.0
Conjunctivitis allergic (10010744)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Cough (10011224)	31	26.3	178	23.5	114	30.5	95	18.9	205	23.9	4	22.2
Croup infectious (10011416)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Cystitis (10011781)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Dermatitis atopic (10012438)	2	1.7	32	4.2	34	9.1	0	0.0	34	4.0	0	0.0
Dermatitis contact (10012442)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Dermatitis diaper (10012444)	0	0.0	6	0.8	6	1.6	0	0.0	6	0.7	0	0.0
Dyspepsia (10013946)	1	0.8	2	0.3	3	0.8	0	0.0	3	0.3	0	0.0
Ear infection (10014011)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Eczema (10014184)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Empyema (10014568)	0	0.0	3	0.4	3	0.8	0	0.0	3	0.3	0	0.0
Enteritis infectious (10058839)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Entropion (10061842)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Eye discharge	1	0.8	1	0.1	2	0.5	0	0.0	2	0.2	0	0.0

Preferred term (code)	Medical History				Concomitant medication				Concomitant vaccination			
	Yes N=118		No N=758		Yes N=374		No N=502		Yes N=858		No N=18	
	n	%	n	%	n	%	n	%	n	%	n	%
(10015915)												
Fungal infection (10017533)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Gastritis (10017853)	1	0.8	7	0.9	8	2.1	0	0.0	8	0.9	0	0.0
Gastroenteritis (10017888)	3	2.5	21	2.8	24	6.4	0	0.0	24	2.8	0	0.0
Gastroenteritis viral (10017918)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Gastrointestinal disorder (10017944)	2	1.7	24	3.2	26	7.0	0	0.0	26	3.0	0	0.0
Gastrooesophageal reflux disease (10017885)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Hypersensitivity (10020751)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Ileus paralytic (10021333)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Influenza (10022000)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Jaundice neonatal (10023138)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Laryngitis (10023874)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Lower respiratory tract infection (10024968)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Milk allergy (10027633)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Nasal congestion (10028735)	1	0.8	2	0.3	3	0.8	0	0.0	3	0.3	0	0.0
Nasopharyngitis (10028810)	9	7.6	70	9.2	79	21.1	0	0.0	78	9.1	1	5.6
Oral candidiasis (10030963)	1	0.8	3	0.4	4	1.1	0	0.0	4	0.5	0	0.0
Otitis externa (10033072)	1	0.8	1	0.1	2	0.5	0	0.0	2	0.2	0	0.0
Otitis media (10033078)	0	0.0	7	0.9	7	1.9	0	0.0	7	0.8	0	0.0
Otitis media acute (10033079)	1	0.8	6	0.8	7	1.9	0	0.0	7	0.8	0	0.0
Pharyngitis (10034835)	0	0.0	10	1.3	10	2.7	0	0.0	10	1.2	0	0.0
Pneumonia (10035664)	0	0.0	3	0.4	3	0.8	0	0.0	3	0.3	0	0.0
Rash (10037844)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Regurgitation (10067171)	1	0.8	0	0.0	1	0.3	0	0.0	1	0.1	0	0.0
Respiratory tract infection (10062352)	0	0.0	2	0.3	2	0.5	0	0.0	2	0.2	0	0.0
Rhinitis (10039083)	0	0.0	8	1.1	8	2.1	0	0.0	8	0.9	0	0.0
Rhinorrhoea (10039101)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Seborrhoeic dermatitis (10039793)	2	1.7	2	0.3	4	1.1	0	0.0	3	0.3	1	5.6
Sepsis (10040047)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Skin lesion (10040882)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Tonsillitis (10044008)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Tremor (10044565)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Tubulointerstitial nephritis (10048302)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Ulcer (10045285)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0

Preferred term (code)	Medical History				Concomitant medication				Concomitant vaccination			
	Yes N=118		No N=758		Yes N=374		No N=502		Yes N=858		No N=18	
	n	%	n	%	n	%	n	%	n	%	n	%
Upper respiratory tract infection (10046306)	4	3.4	20	2.6	24	6.4	0	0.0	24	2.8	0	0.0
Urethritis (10046480)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Urinary tract infection (10046571)	0	0.0	1	0.1	1	0.3	0	0.0	1	0.1	0	0.0
Urticaria (10046735)	0	0.0	4	0.5	4	1.1	0	0.0	4	0.5	0	0.0
Total	**51**	**43.2**	**354**	**46.7**	**310**	**82.9**	**95**	**18.9**	**401**	**46.7**	**4**	**22.2**

N = Number of subjects
n (%) = number (percentage) of subjects with the specified category
* The classification of adverse events as expected & unexpected AEs is done by Low level term code mentioned in the cleaning report of this study.
Total = number (percentage) of subjects with at least one AE reported, irrespective of the classification

A.6 Adverse event by adverse event duration

Table 21 presents the expected and unexpected AEs by duration for the Total Vaccinated cohort.

Expected AEs:

Post Dose 1 of Rotarix™:

- Of the 349 cases of irritability reported, 102 (29.2%) cases lasted for a day, 89 (25.5%) cases lasted for 2 days, 65 (18.6%) cases lasted for 3 days and 93 (26.6%) cases lasted for 4 to 7 days after vaccination.

- Of the 208 cases of decreased appetite reported, 57 (27.4%) cases lasted for a day, 52 (25.0%) cases lasted for 2 days, 42 (20.2%) cases lasted for 3 days and 57 (27.4%) cases lasted for 4 to 7 days after vaccination.

- Of the 166 cases of vomiting reported, 55 (33.1%) cases lasted for a day, 30 (18.1%) cases lasted for 2 days, 27 (16.3%) cases lasted for 3 days and 54 (32.5.%) cases lasted for 4 to 7 days after vaccination.

Post Dose 2 of Rotarix™:

- Of the 139 cases of irritability reported, 45 (32.4%) cases lasted for a day, 47 (33.8%) cases lasted for 2 days, 19 (13.7%) cases lasted for 3 days and 28 (20.1%) cases lasted for 4 to 7 days after vaccination.

- Of the 88 cases of decreased appetite reported, 29 (33.0%) cases lasted for a day, 21 (23.9%) cases lasted for 2 days, 12 (13.6%) cases lasted for 3 days and 26 (29.5%) cases lasted for 4 to 7 days after vaccination.

- Of the 58 cases of vomiting reported, 15 (25.9%) cases lasted for a day, 10 (17.2%) cases lasted for 2 days, 11 (19.0%) cases lasted for 3 days and 22(37.9)cases lasted for 4 to 7 days after vaccination.

Unexpected AEs:

Post Dose 1 of Rotarix™:

- Of the 153 cases of cough reported, 44 (28.8%) cases lasted for a day, 31 (20.3%) cases lasted for 2 days, 25 (16.3%) cases lasted for 3 days, 41 (26.8%) cases lasted for 4 to 7 days after vaccination. Twelve (7.8%) cases of cough lasted for 8 to 15 days after vaccination.
- Of the 39 cases of nasopharyngitis reported, 5 (12.8%) cases lasted for 2 days, 16 (41.0%) cases lasted for 3 days, 13 (33.3%) cases lasted for 4 to 7 days and 4 (10.3%) cases lasted for 8 to 15 days after vaccination. One (2.6%) case of nasopharyngitis reported lasted for more than 30 days after vaccination.
- Of the 45 cases of bronchiolitis reported, 3 (6.7%) cases lasted for 2 days, 12 (26.7%) cases lasted for 3 days, 17 (37.8%) cases lasted for 4 to 7 days, 9

(20.0%) cases lasted for 8 to 15 days, 2 (4.4%) cases lasted for 16 to 30 days after vaccination. Two (4.4%) cases of bronchiolitis reported lasted for more than 30 days after vaccination.

Post Dose 2 of Rotarix™:

- Of the 90 cases of cough reported, 19 (21.1%) cases lasted for a day, 20 (22.2%) cases lasted for 2 days, 12 (13.3%) cases lasted for 3 days and 26 (28.9%) cases lasted for 4 to 7 days after vaccination. Thirteen (14.4%) cases of cough lasted for 8 to 15 days after vaccination.
- Of the 60 cases of nasopharyngitis reported, 8 (13.3%) cases lasted for 2 days, 26 (43.3%) cases lasted for 3 days, 23 (38.3%) cases lasted for 4 to 7 days and 2 (3.3%) cases lasted for 8 to 15 days after vaccination. One (1.7%) case of nasopharyngitis lasted for 16 to 30 days after vaccination.
- Of the 33 cases of bronchiolitis reported, 6 (18.2%) cases lasted for 2 days, 12 (36.4%) cases lasted for 3 days and 11 (33.3%) cases lasted for 4 to 7 days after vaccination. Four (12.1%) cases of bronchiolitis lasted for 8 to 15 days after vaccination.

Table 21 Expected & Unexpected adverse events by duration (Total Vaccinated cohort)

			DAY 0		DAY 1		DAY 2		DAY 3		DAY 4-7		DAY 8-15		DAY 16-30		DAY >30	
Preferred term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Expected adverse events by duration*																		
Constipation (10010774)	1	3	0	0	0	0	2	66.7	1	33.3	0	0	0	0	0	0	0	0
	2	2	0	0	0	0	0	0	0	0	2	100.0	0	0	0	0	0	0
Decreased appetite (10061428)	1	208	0	0	57	27.4	52	25.0	42	20.2	57	27.4	0	0	0	0	0	0
	2	88	0	0	29	33.0	21	23.9	12	13.6	26	29.5	0	0	0	0	0	0
Dermatitis (10012431)	1	8	0	0	2	25.0	1	12.5	2	25.0	3	37.5	0	0	0	0	0	0
	2	4	0	0	1	25.0	2	50.0	0	0	1	25.0	0	0	0	0	0	0
Diarrhoea (10012735)	1	39	0	0	14	35.9	9	23.1	3	7.7	12	30.8	1	2.6	0	0	0	0
	2	17	0	0	9	52.9	2	11.8	3	17.6	3	17.6	0	0	0	0	0	0
Irritability (10022998)	1	349	0	0	102	29.2	89	25.5	65	18.6	93	26.6	0	0	0	0	0	0
	2	139	0	0	45	32.4	47	33.8	19	13.7	28	20.1	0	0	0	0	0	0
Pyrexia (10037660)	1	115	0	0	64	55.7	30	26.1	10	8.7	11	9.6	0	0	0	0	0	0
	2	35	0	0	13	37.1	14	40.0	3	8.6	5	14.3	0	0	0	0	0	0
Rash (10037844)	1	2	0	0	0	0	1	50.0	1	50.0	0	0	0	0	0	0	0	0
Rhinorrhoea (10039101)	1	3	0	0	0	0	0	0	2	66.7	1	33.3	0	0	0	0	0	0
	2	3	0	0	0	0	0	0	2	66.7	1	33.3	0	0	0	0	0	0
Upper respiratory tract infection (10046306)	1	36	0	0	1	2.8	7	19.4	9	25.0	14	38.9	4	11.1	1	2.8	0	0
	2	29	0	0	0	0	1	3.4	14	48.3	11	37.9	2	6.9	1	3.4	0	0
Vomiting (10047700)	1	166	0	0	55	33.1	30	18.1	27	16.3	54	32.5	0	0	0	0	0	0
	2	58	0	0	15	25.9	10	17.2	11	19.0	22	37.9	0	0	0	0	0	0
Unexpected adverse events by duration*																		
Acute sinusitis (10001076)	1	2	0	0	0	0	0	0	1	50.0	1	50.0	0	0	0	0	0	0
	2	1	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0
Acute tonsillitis (10001093)	1	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
	2	3	0	0	0	0	0	0	1	33.3	1	33.3	1	33.3	0	0	0	0
Asthma (10003553)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
	2	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Atopy (10003645)	1	3	0	0	1	33.3	1	33.3	0	0	1	33.3	0	0	0	0	0	0
	2	3	0	0	2	66.7	0	0	0	0	0	0	1	33.3	0	0	0	0
Balanoposthitis (10004078)	2	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Bronchiolitis (10006448)	1	45	0	0	0	0	3	6.7	12	26.7	17	37.8	9	20.0	2	4.4	2	4.4

			DAY 0		DAY 1		DAY 2		DAY 3		DAY 4-7		DAY 8-15		DAY 16-30		DAY >30	
Preferred term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	2	33	0	0	0	0	6	18.2	12	36.4	11	33.3	4	12.1	0	0	0	0
Bronchitis (10006451)	1	6	0	0	0	0	3	50.0	0	0	1	16.7	2	33.3	0	0	0	0
	2	6	0	0	0	0	0	0	3	50.0	2	33.3	1	16.7	0	0	0	0
Cellulitis (10007882)	1	1	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0	0	0
	2	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Colitis (10009887)	1	2	0	0	0	0	1	50.0	0	0	1	50.0	0	0	0	0	0	0
Conjunctivitis (10010741)	1	5	0	0	1	20.0	0	0	1	20.0	2	40.0	0	0	1	20.0	0	0
	2	2	0	0	1	50.0	0	0	0	0	1	50.0	0	0	0	0	0	0
Conjunctivitis allergic (10010744)	1	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Cough (10011224)	1	153	0	0	44	28.8	31	20.3	25	16.3	41	26.8	12	7.8	0	0	0	0
	2	90	0	0	19	21.1	20	22.2	12	13.3	26	28.9	13	14.4	0	0	0	0
Croup infectious (10011416)	2	1	0	0	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0
Cystitis (10011781)	2	1	0	0	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0
Dermatitis atopic (10012438)	1	23	0	0	2	8.7	7	30.4	3	13.0	10	43.5	0	0	1	4.3	0	0
	2	14	0	0	0	0	8	57.1	3	21.4	3	21.4	0	0	0	0	0	0
Dermatitis contact (10012442)	2	2	0	0	0	0	0	0	1	50.0	1	50.0	0	0	0	0	0	0
Dermatitis diaper (10012444)	2	6	0	0	2	33.3	1	16.7	2	33.3	1	16.7	0	0	0	0	0	0
Dyspepsia (10013946)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
	2	2	0	0	0	0	0	0	1	50.0	1	50.0	0	0	0	0	0	0
Ear infection (10014011)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Eczema (10014184)	1	2	0	0	1	50.0	1	50.0	0	0	0	0	0	0	0	0	0	0
Empyema (10014568)	1	2	0	0	0	0	1	50.0	1	50.0	0	0	0	0	0	0	0	0
	2	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Enteritis infectious (10058839)	2	1	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0
Entropion (10061842)	2	1	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0	0	0
Eye discharge (10015915)	1	2	0	0	1	50.0	0	0	0	0	1	50.0	0	0	0	0	0	0
Fungal infection (10017533)	2	1	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0	0	0
Gastritis (10017853)	1	6	0	0	0	0	4	66.7	2	33.3	0	0	0	0	0	0	0	0
	2	4	0	0	0	0	0	0	3	75.0	1	25.0	0	0	0	0	0	0
Gastroenteritis (10017888)	1	22	0	0	0	0	8	36.4	1	4.5	9	40.9	1	4.5	2	9.1	1	4.5
	2	7	0	0	0	0	2	28.6	3	42.9	2	28.6	0	0	0	0	0	0
Gastroenteritis viral (10017918)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
	2	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Gastrointestinal disorder	1	19	0	0	0	0	9	47.4	3	15.8	4	21.1	3	15.8	0	0	0	0

			DAY 0		DAY 1		DAY 2		DAY 3		DAY 4-7		DAY 8-15		DAY 16-30		DAY >30	
Preferred term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
(10017944)																		
	2	8	0	0	0	0	3	37.5	2	25.0	2	25.0	1	12.5	0	0	0	0
Gastrooesophageal reflux disease (10017885)	1	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
	2	1	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0
Hypersensitivity (10020751)	2	2	0	0	0	0	0	0	1	50.0	1	50.0	0	0	0	0	0	0
Ileus paralytic (10021333)	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	100.0	0	0
Influenza (10022000)	2	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Jaundice neonatal (10023138)	2	1	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0
Laryngitis (10023874)	2	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Lower respiratory tract infection (10024968)	1	2	0	0	0	0	1	50.0	1	50.0	0	0	0	0	0	0	0	0
	2	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Milk allergy (10027633)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Nasal congestion (10028735)	1	3	0	0	0	0	0	0	2	66.7	1	33.3	0	0	0	0	0	0
Nasopharyngitis (10028810)	1	39	0	0	0	0	5	12.8	16	41.0	13	33.3	4	10.3	0	0	1	2.6
	2	60	0	0	0	0	8	13.3	26	43.3	23	38.3	2	3.3	1	1.7	0	0
Oral candidiasis (10030963)	1	4	0	0	0	0	0	0	0	0	2	50.0	2	50.0	0	0	0	0
	2	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Otitis externa (10033072)	1	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
	2	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Otitis media (10033078)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
	2	6	0	0	0	0	1	16.7	2	33.3	2	33.3	1	16.7	0	0	0	0
Otitis media acute (10033079)	1	3	0	0	0	0	0	0	1	33.3	1	33.3	0	0	0	0	1	33.3
	2	5	0	0	0	0	0	0	0	0	0	0	4	80.0	1	20.0	0	0
Pharyngitis (10034835)	1	9	0	0	0	0	1	11.1	4	44.4	4	44.4	0	0	0	0	0	0
	2	4	0	0	0	0	0	0	4	100.0	0	0	0	0	0	0	0	0
Pneumonia (10035664)	1	3	0	0	0	0	0	0	0	0	0	0	3	100.0	0	0	0	0
Rash (10037844)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Regurgitation (10067171)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Respiratory tract infection (10062352)	1	3	0	0	0	0	2	66.7	1	33.3	0	0	0	0	0	0	0	0
	2	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0
Rhinitis (10039083)	1	5	0	0	0	0	0	0	2	40.0	1	20.0	1	20.0	0	0	1	20.0

			DAY 0		DAY 1		DAY 2		DAY 3		DAY 4-7		DAY 8-15		DAY 16-30		DAY >30	
Preferred term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	2	7	0	0	0	0	0	0	6	85.7	1	14.3	0	0	0	0	0	0
Rhinorrhoea (10039101)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0
Seborrhoeic dermatitis (10039793)	1	3	0	0	1	33.3	0	0	0	0	1	33.3	0	0	1	33.3	0	0
	2	2	0	0	0	0	0	0	1	50.0	1	50.0	0	0	0	0	2	0
Sepsis (10040047)	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	100.0	1	0
Skin lesion (10040882)	2	1	0	0	1	100.0	0	0	0	0	0	0	0	0	0	0	2	0
Tonsillitis (10044008)	1	1	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0	1	0
	2	1	0	0	0	0	1	100.0	0	0	0	0	0	0	0	0	2	0
Tremor (10044565)	2	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	2	0
Tubulointerstitial nephritis (10048302)	2	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	2	0
Ulcer (10045285)	2	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	2	0
Upper respiratory tract infection (10046306)	1	12	0	0	2	16.7	0	0	2	16.7	4	33.3	3	25.0	1	8.3	1	0
	2	13	0	0	1	7.7	1	7.7	2	15.4	9	69.2	0	0	0	0	2	0
Urethritis (10046480)	1	1	0	0	0	0	0	0	1	100.0	0	0	0	0	0	0	1	0
Urinary tract infection (10046571)	1	1	0	0	0	0	0	0	0	0	1	100.0	0	0	0	0	1	0
Urticaria (10046735)	1	2	0	0	0	0	0	0	1	50.0	1	50.0	0	0	0	0	1	0
	2	2	0	0	0	0	0	0	0	0	2	100.0	0	0	0	0	2	0

N = Number of events

n (%) = number (percentage)of events with the specified category

* The classification of adverse events as Expected & Unexpected AEs is done by Low level term code mentioned in the cleaning report of this study.

B. Adverse events in special subpopulations

B.1 Old people (65 years or more)

Not applicable.

B.2 Infant

Not applicable.

B.3 Pregnant or nursing mother

Not applicable.

B.4 Patients with renal impairment

Not applicable.

B.5 Patients with hepatic impairment

Not applicable.

C. Factors considered as affecting the manifestation of adverse events

The analysis is not applicable for this time point and will be done for the cumulative report.

5.1.5 Classification of adverse events

A. Severity

Table 22 presents the expected and unexpected AEs by severity for the Total Vaccinated cohort.

Expected AEs

Post Dose 1 of Rotarix™:

- Of the 349 cases of irritability reported, 220 (63.0%) cases were assessed as mild, 103 (29.5%) cases were assessed as moderate and only 26 (7.4%) cases of irritability were assessed as severe.
- Of the 208 cases of decreased appetite reported, 174 (83.7%) cases were assessed as mild, 31 (14.9%) cases were assessed as moderate and only 3 (1.4%) cases of decreased appetitewere assessed as severe.

- Of the 166 cases of vomiting reported, 83 (50.3%) cases were assessed as mild, 42 (25.5%) cases were assessed as moderate and only 40 (24.2%) cases of vomiting were assessed as severe.
- Of the 115 cases of pyrexia reported, 83 (72.2%) cases were assessed as mild, 29 (25.2%) cases were assessed as moderate and only 3 (2.6%) cases of pyrexia were assessed as severe.
- Of the 39 cases of diarrhoea reported, 21 (55.3%) cases were assessed as mild, 14 (36.8%) cases were assessed as moderate and only 3 (7.9%) cases of diarrhoea were assessed as severe.

Post Dose 2 of Rotarix™:

- Of the 139 cases of irritability reported, 95 (68.3%) cases were assessed as mild, 39 (28.1%) cases were assessed as moderate and only 5 (3.6%) cases of irritability were assessed as severe.
- Of the 88 cases of decreased appetite reported, 75 (85.2%) cases were assessed as mild, 12 (13.6%) cases were assessed as moderate and only one (1.1%) case of decreased appetite were assessed as severe.
- Of the 58 cases of vomiting reported, 24 (42.1%) cases were assessed as mild, 17 (29.8%) cases were assessed as moderate and only 16 (28.1%) cases of vomiting were assessed as severe.
- Of the 35 cases of pyrexia reported, 27(77.1%) cases were assessed as mild and 8 (22.9%) cases were assessed as moderate. None of the cases were assessed as severe.
- Of the 17 cases of diarrhoea reported, 11 (64.7%) cases were assessed as mild, 4 (23.5%) cases were assessed as moderate and only 2 (11.8%) cases of diarrhoea were assessed as severe.

<u>Unexpected AEs</u>

Post Dose 1 of Rotarix™:

- Of the 153 cases of cough reported, 132 (86.8%) cases were assessed as mild, 19 (12.4%) cases were assessed as moderate and only one (0.7%) case of cough was assessed as severe.
- Of the 45 cases of bronchiolitis reported, 30 (66.7%) cases were assessed as mild, 14 (31.1%) cases were assessed as moderate and only one (2.2%) case of bronchiolitis was assessed as severe.
- Of the 22 cases of GE reported, 17 (77.3%) cases of GE were assessed as mild, 4 (18.2%) cases of GE were assessed as moderate and only one (4.5%) case of GE was assessed as severe.
- Of the 3 cases of otitis media acute reported, 2 (66.7%) cases were assessed as mild and only one (33.3%) case of AOM was assessed as severe.

Post Dose 2 of Rotarix™:

- Of the 90 cases of cough reported, 72 (80.0%) cases were assessed as mild, 17 (18.9%) cases were assessed as moderate and only one (1.1%) case of cough was assessed as severe.
- Of the 33 cases of bronchiolitis reported, 25 (75.8%) cases were assessed as mild and 8 (24.2%) cases were assessed as moderate. None of the cases of bronchiolitis reported post Dose 2 of Rotarix™were assessed as severe.
- Of the 7 cases of GE reported, 4 (57.1%) cases were assessed as mild, 3 (42.9%) cases were assessed as moderate. None of the cases of GE reported post Dose 2 of Rotarix™ were assessed as severe.
- Of the 5 cases of otitis media acute reported, 2 (40.0%) cases were assessed as mild and 3 (60.0%) cases were assessed as moderate. None of the cases of otitis media aute reported post Dose 2 of Rotarix™ were assessed as severe.

Table 22 Expected & Unexpected adverse events by severity (Total Vaccinated cohort)

			Mild		Moderate		Severe	
Preferred Term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
Expected adverse events by severity*								
Constipation (10010774)	1	3	2	66.7	1	33.3	0	0.0
	2	2	2	100	0	0.0	0	0.0
Decreased appetite (10061428)	1	208	174	83.7	31	14.9	3	1.4
	2	88	75	85.2	12	13.6	1	1.1
Dermatitis (10012431)	1	8	8	100	0	0.0	0	0.0
	2	4	4	100	0	0.0	0	0.0
Diarrhoea (10012735)	1	39	21	55.3	14	36.8	3	7.9
	2	17	11	64.7	4	23.5	2	11.8
Irritability (10022998)	1	349	220	63.0	103	29.5	26	7.4
	2	139	95	68.3	39	28.1	5	3.6
Pyrexia (10037660)	1	115	83	72.2	29	25.2	3	2.6
	2	35	27	77.1	8	22.9	0	0.0
Rash (10037844)	1	2	2	100	0	0.0	0	0.0
Rhinorrhoea (10039101)	1	3	3	100	0	0.0	0	0.0
	2	3	2	66.7	1	33.3	0	0.0
Upper respiratory tract infection (10046306)	1	36	30	83.3	6	16.7	0	0.0
	2	29	24	82.8	5	17.2	0	0.0
Vomiting (10047700)	1	166	83	50.3	42	25.5	40	24.2
	2	58	24	42.1	17	29.8	16	28.1
Unexpected adverse events by severity*								
Acute sinusitis (10001076)	1	2	1	50.0	1	50.0	0	0.0
	2	1	1	100	0	0.0	0	0.0

			Mild		Moderate		Severe	
Preferred Term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
Acute tonsillitis (10001093)	1	1	1	100	0	0.0	0	0.0
	2	3	2	66.7	1	33.3	0	0.0
Asthma (10003553)	1	1	0	0.0	1	100	0	0.0
	2	1	1	100	0	0.0	0	0.0
Atopy (10003645)	1	3	3	100	0	0.0	0	0.0
	2	3	3	100	0	0.0	0	0.0
Balanoposthitis (10004078)	2	1	1	100	0	0.0	0	0.0
Bronchiolitis (10006448)	1	45	30	66.7	14	31.1	1	2.2
	2	33	25	75.8	8	24.2	0	0.0
Bronchitis (10006451)	1	6	3	50.0	3	50.0	0	0.0
	2	6	6	100	0	0.0	0	0.0
Cellulitis (10007882)	1	1	1	100	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0
Colitis (10009887)	1	2	1	50.0	1	50.0	0	0.0
Conjunctivitis (10010741)	1	5	5	100	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0
Conjunctivitis allergic (10010744)	1	1	1	100	0	0.0	0	0.0
Cough (10011224)	1	153	132	86.3	19	12.4	1	0.7
	2	90	72	80.0	17	18.9	1	1.1
Croup infectious (10011416)	2	1	0	0.0	1	100	0	0.0
Cystitis (10011781)	2	1	0	0.0	1	100	0	0.0
Dermatitis atopic (10012438)	1	23	22	95.7	1	4.3	0	0.0
	2	14	13	92.9	1	7.1	0	0.0
Dermatitis contact (10012442)	2	2	2	100	0	0.0	0	0.0
Dermatitis diaper (10012444)	2	6	6	100	0	0.0	0	0.0
Dyspepsia (10013946)	1	1	1	100	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0
Ear infection (10014011)	1	1	1	100	0	0.0	0	0.0
Eczema (10014184)	1	2	2	100	0	0.0	0	0.0
Empyema (10014568)	1	2	1	50.0	1	50.0	0	0.0
	2	1	1	100	0	0.0	0	0.0
Enteritis infectious (10058839)	2	1	1	100	0	0.0	0	0.0
Entropion (10061842)	2	1	1	100	0	0.0	0	0.0
Eye discharge (10015915)	1	2	2	100	0	0.0	0	0.0
Fungal infection (10017533)	2	1	0	0.0	1	100	0	0.0

			Mild		Moderate		Severe	
Preferred Term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
Gastritis (10017853)	1	6	3	50.0	3	50.0	0	0.0
	2	4	3	75.0	1	25.0	0	0.0
Gastroenteritis (10017888)	1	22	17	77.3	4	18.2	1	4.5
	2	7	4	57.1	3	42.9	0	0.0
Gastroenteritis viral (10017918)	1	1	0	0.0	1	100	0	0.0
	2	1	0	0.0	1	100	0	0.0
Gastrointestinal disorder (10017944)	1	19	16	84.2	3	15.8	0	0.0
	2	8	7	87.5	1	12.5	0	0.0
Gastrooesophageal reflux disease (10017885)	1	1	1	100	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0
Hypersensitivity (10020751)	2	2	2	100	0	0.0	0	0.0
Ileus paralytic (10021333)	1	1	0	0.0	1	100	0	0.0
Influenza (10022000)	2	1	1	100	0	0.0	0	0.0
Jaundice neonatal (10023138)	2	1	0	0.0	1	100	0	0.0
Laryngitis (10023874)	2	1	1	100	0	0.0	0	0.0
Lower respiratory tract infection (10024968)	1	2	0	0.0	2	100	0	0.0
	2	1	0	0.0	1	100	0	0.0
Milk allergy (10027633)	1	1	1	100	0	0.0	0	0.0
Nasal congestion (10028735)	1	3	2	66.7	1	33.3	0	0.0
Nasopharyngitis (10028810)	1	39	35	89.7	4	10.3	0	0.0
	2	60	46	76.7	14	23.3	0	0.0
Oral candidiasis (10030963)	1	4	2	50.0	2	50.0	0	0.0
	2	1	1	100	0	0.0	0	0.0
Otitis externa (10033072)	1	1	1	100	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0
Otitis media (10033078)	1	1	1	100	0	0.0	0	0.0
	2	6	5	83.3	1	16.7	0	0.0
Otitis media acute (10033079)	1	3	2	66.7	0	0.0	1	33.3
	2	5	2	40.0	3	60.0	0	0.0
Pharyngitis (10034835)	1	9	7	77.8	2	22.2	0	0.0
	2	4	4	100	0	0.0	0	0.0
Pneumonia (10035664)	1	3	1	33.3	2	66.7	0	0.0

			Mild		Moderate		Severe	
Preferred Term (code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
Rash (10037844)	1	1	1	100	0	0.0	0	0.0
Regurgitation (10067171)	1	1	1	100	0	0.0	0	0.0
Respiratory tract infection (10062352)	1	3	0	0.0	3	100	0	0.0
	2	1	0	0.0	1	100	0	0.0
Rhinitis (10039083)	1	5	3	60.0	2	40.0	0	0.0
	2	7	4	57.1	3	42.9	0	0.0
Rhinorrhoea (10039101)	1	1	1	100	0	0.0	0	0.0
Seborrhoeic dermatitis (10039793)	1	3	3	100	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0
Sepsis (10040047)	1	1	1	100	0	0.0	0	0.0
Skin lesion (10040882)	2	1	1	100	0	0.0	0	0.0
Tonsillitis (10044008)	1	1	1	100	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0
Tremor (10044565)	2	1	1	100	0	0.0	0	0.0
Tubulointerstitial nephritis (10048302)	2	1	1	100	0	0.0	0	0.0
Ulcer (10045285)	2	1	1	100	0	0.0	0	0.0
Upper respiratory tract infection (10046306)	1	12	9	75.0	3	25.0	0	0.0
	2	13	12	92.3	1	7.7	0	0.0
Urethritis (10046480)	1	1	1	100	0	0.0	0	0.0
Urinary tract infection (10046571)	1	1	1	100	0	0.0	0	0.0
Urticaria (10046735)	1	2	2	100	0	0.0	0	0.0
	2	2	1	50.0	1	50.0	0	0.0

N = Number of events
n (%) = number (percentage)of events with the specified category
* The classification of adverse events as Expected & Unexpected AEs is done by Low level term code mentioned in the cleaning report of this study.

B. Causal relationship with the survey vaccine

Table 23 presents the expected and unexpected AEs by causality for the Total Vaccinated cohort.

Expected AEs:

Post Dose 1 of Rotarix™:

- Of the 349 cases of irritability reported, one (0.3%) case of irritability was assessed as definitely related, 9 (2.6%) cases as probably related and 30 (8.6%) cases as possibly related to vaccination.
- Of the 208 cases of decreased appetite reported, one (0.5%) case of decreased appetitewas assessed as definitely related, 3 (1.4%) cases as probably related and 14 (6.7%) cases as possibly related to vaccination.
- Of the 166 cases of vomiting reported, three (1.8%) cases of vomiting were assessed as definitely related, 5 (3.0%) cases as probably related and 29 (17.5%) cases as possibly related to vaccination.
- Of the 115 cases of pyrexia reported, one (0.9%) case of pyrexia was assessed as definitely related, 5 (4.3%) cases as probably related and 17 (14.8%) cases as possibly related to vaccination.
- Of the 39 cases of diarrhoea reported, 2 (5.1%) cases of diarrhoea were assessed as definitely related, one (2.6%) case as probably related and 10 (25.6%) cases as possibly related to vaccination.

Post Dose 2 of Rotarix™:

- Of the 139 cases of irritability reported, one (0.7%) case of irritability was assessed as definitely related, 2 (1.4%) cases as probably related and 10 (7.2%) cases as possibly related to vaccination.
- Of the 88 cases of decreased appetite reported, 2 (2.3%) cases of decreased appetite were assessed as probably related and 6 (6.8%) cases as possibly related to vaccination.
- Of the 58 cases of vomiting reported, one (1.7%) case of vomiting was assessed as probably related and 5 (8.6%) cases as possibly related to vaccination.
- Of the 35 cases of pyrexia reported, 6 (17.1%) cases of pyrexia were assessed as possibly related to vaccination.
- Of the 17 cases of diarrhoea reported, 3 (17.6%) cases of diarrhoea were assessed as possibly related to vaccination.

Unexpected AEs:

Post Dose 1 of Rotarix™:

- Of the 153 cases of cough reported, 4 (2.6%) cases were assessed as possibly related to vaccination and 3 (2.0%) cases of cough were assessed as unknown.
- Of the 22 cases of GE reported one (4.5%) case was assessed as possibly related to vaccination.
- Of the 19 cases of gastrointestinal disorders reported two (10.5%) cases were assessed as possibly related to vaccination.

Post Dose 2 of Rotarix™:

- Of the 90 cases of cough reported, one (1.1%) case was assessed as possibly related to vaccination and 3 (3.3%) cases of cough were assessed as unknown.

- Of the 33 cases of bronchiolitis reported, one (3.0%) case of bronchiolitis was assessed as possibly related to vaccination and one (3.0%) case of bronchiolitis was assessed as unknown.
- One (50.0%) case of utricaria was assessed as probably related to vaccination.
- Of the 8 cases of gastrointestinal disorders reported 1 (12.5%) case was assessed as probably related to vaccination.

Table 23 Expected & Unexpected adverse events by causality (Total Vaccinated cohort)

			Definitely related		Probably related		Possibly related		Probably not related		Unknown	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Expected adverse events by causality*												
Constipation (10010774)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
	2	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Decreased appetite (10061428)	1	208	1	0.5	3	1.4	14	6.7	190	91.3	0	0.0
	2	88	0	0.0	2	2.3	6	6.8	80	90.9	0	0.0
Dermatitis (10012431)	1	8	0	0.0	0	0.0	0	0.0	8	100	0	0.0
	2	4	0	0.0	0	0.0	0	0.0	4	100	0	0.0
Diarrhoea (10012735)	1	39	2	5.1	1	2.6	10	25.6	26	66.7	0	0.0
	2	17	0	0.0	0	0.0	3	17.6	14	82.4	0	0.0
Irritability (10022998)	1	349	1	0.3	9	2.6	30	8.6	309	88.5	0	0.0
	2	139	1	0.7	2	1.4	10	7.2	126	90.6	0	0.0
Pyrexia (10037660)	1	115	1	0.9	5	4.3	17	14.8	92	80.0	0	0.0
	2	35	0	0.0	0	0.0	6	17.1	29	82.9	0	0.0
Rash (10037844)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Rhinorrhoea (10039101)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
	2	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
Upper respiratory tract infection (10046306)	1	36	0	0.0	0	0.0	0	0.0	36	100	0	0.0
	2	29	0	0.0	0	0.0	0	0.0	29	100	0	0.0
Vomiting (10047700)	1	166	3	1.8	5	3.0	29	17.5	127	76.5	2	1.2
	2	58	0	0.0	1	1.7	5	8.6	52	89.7	0	0.0
Unexpected adverse events by causality*												
Acute sinusitis (10001076)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Acute tonsillitis (10001093)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
Asthma (10003553)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Atopy (10003645)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
	2	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0

			Definitely related		Probably related		Possibly related		Probably not related		Unknown	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Balanoposthitis (10004078)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Bronchiolitis (10006448)	1	45	0	0.0	0	0.0	0	0.0	45	100	0	0.0
	2	33	0	0.0	0	0.0	1	3.0	31	93.9	1	3.0
Bronchitis (10006451)	1	6	0	0.0	0	0.0	0	0.0	6	100	0	0.0
	2	6	0	0.0	0	0.0	0	0.0	6	100	0	0.0
Cellulitis (10007882)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Colitis (10009887)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Conjunctivitis (10010741)	1	5	0	0.0	0	0.0	0	0.0	5	100	0	0.0
	2	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Conjunctivitis allergic (10010744)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Cough (10011224)	1	153	0	0.0	0	0.0	4	2.6	145	94.8	3	2.0
	2	90	0	0.0	0	0.0	1	1.1	86	95.6	3	3.3
Croup infectious (10011416)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Cystitis (10011781)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Dermatitis atopic (10012438)	1	23	0	0.0	0	0.0	0	0.0	23	100	0	0.0
	2	14	0	0.0	0	0.0	1	7.1	13	92.9	0	0.0
Dermatitis contact (10012442)	2	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Dermatitis diaper (10012444)	2	6	0	0.0	0	0.0	0	0.0	6	100	0	0.0
Dyspepsia (10013946)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Ear infection (10014011)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Eczema (10014184)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Empyema (10014568)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Enteritis infectious (10058839)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Entropion (10061842)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Eye discharge (10015915)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Fungal infection (10017533)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Gastritis (10017853)	1	6	0	0.0	0	0.0	0	0.0	6	100	0	0.0
	2	4	0	0.0	0	0.0	0	0.0	4	100	0	0.0
Gastroenteritis (10017888)	1	22	0	0.0	0	0.0	1	4.5	21	95.5	0	0.0
	2	7	0	0.0	0	0.0	0	0.0	7	100	0	0.0

			Definitely related		Probably related		Possibly related		Probably not related		Unknown	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Gastroenteritis viral (10017918)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Gastrointestinal disorder (10017944)	1	19	0	0.0	0	0.0	2	10.5	17	89.5	0	0.0
	2	8	0	0.0	1	12.5	0	0.0	7	87.5	0	0.0
Gastrooesophageal reflux disease (10017885)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Hypersensitivity (10020751)	2	2	0	0.0	0	0.0	1	50.0	1	50.0	0	0.0
Ileus paralytic (10021333)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Influenza (10022000)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Jaundice neonatal (10023138)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Laryngitis (10023874)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Lower respiratory tract infection (10024968)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Milk allergy (10027633)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Nasal congestion (10028735)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
Nasopharyngitis (10028810)	1	39	0	0.0	0	0.0	0	0.0	39	100	0	0.0
	2	60	0	0.0	0	0.0	0	0.0	60	100	0	0.0
Oral candidiasis (10030963)	1	4	0	0.0	0	0.0	0	0.0	4	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Otitis externa (10033072)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Otitis media (10033078)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	6	0	0.0	0	0.0	1	16.7	5	83.3	0	0.0
Otitis media acute (10033079)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
	2	5	0	0.0	0	0.0	0	0.0	5	100	0	0.0
Pharyngitis (10034835)	1	9	0	0.0	0	0.0	0	0.0	9	100	0	0.0
	2	4	0	0.0	0	0.0	0	0.0	4	100	0	0.0
Pneumonia (10035664)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
Rash (10037844)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Regurgitation (10067171)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0

			Definitely related		Probably related		Possibly related		Probably not related		Unknown	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Respiratory tract infection (10062352)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Rhinitis (10039083)	1	5	0	0.0	0	0.0	0	0.0	5	100	0	0.0
	2	7	0	0.0	0	0.0	0	0.0	7	100	0	0.0
Rhinorrhoea (10039101)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Seborrhoeic dermatitis (10039793)	1	3	0	0.0	0	0.0	0	0.0	3	100	0	0.0
	2	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
Sepsis (10040047)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Skin lesion (10040882)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Tonsillitis (10044008)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Tremor (10044565)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Tubulointerstitial nephritis (10048302)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Ulcer (10045285)	2	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Upper respiratory tract infection (10046306)	1	12	0	0.0	0	0.0	0	0.0	10	83.3	2	16.7
	2	13	0	0.0	0	0.0	0	0.0	10	76.9	3	23.1
Urethritis (10046480)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Urinary tract infection (10046571)	1	1	0	0.0	0	0.0	0	0.0	1	100	0	0.0
Urticaria (10046735)	1	2	0	0.0	0	0.0	0	0.0	2	100	0	0.0
	2	2	0	0.0	1	50.0	0	0.0	1	50.0	0	0.0

N = Number of events
n(%) = number (percentage)of events with the specified category
* The classification of adverse events as Expected & Unexpected AEs is done by Low level term code mentioned in the cleaning report of this study.

C. Results of adverse events

Table 24 presents the expected and unexpected AEs by outcome for the Total Vaccinated cohort.

Expected AEs

- All the expected AEs had resolved by the end of the study period.

Unexpected AEs

Of the unexpected AEs reported, one (1.7%) case of nasopharyngitis and one (20.0%) case of otitis media acute were reported and resolved with sequelae.

Table 24 Expected & Unexpected adverse events by outcome (Total Vaccinated cohort)

			Recovered /Resolved		Recovering /Resolving		Not recovered / not resolved		Recovered / Resolved with sequelqe	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Expected adverse events by outcome*										
Constipation (10010774)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0	0	0.0
Dermatitis (10012431)	1	8	8	100	0	0.0	0	0.0	0	0.0
	2	4	4	100	0	0.0	0	0.0	0	0.0
Diarrhoea (10012735)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0	0	0.0
Pyrexia (10037660)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0	0	0.0
Rash (10037844)	1	2	2	100	0	0.0	0	0.0	0	0.0
Rhinorrhoea (10039101)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	3	3	100	0	0.0	0	0.0	0	0.0
Upper respiratory tract infection (10046306)	1	36	36	100	0	0.0	0	0.0	0	0.0
	2	29	29	100	0	0.0	0	0.0	0	0.0
Unexpected adverse events by outcome*										
Acute sinusitis (10001076)	1	2	2	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Acute tonsillitis (10001093)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	3	3	100	0	0.0	0	0.0	0	0.0
Asthma (10003553)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Atopy (10003645)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	3	3	100	0	0.0	0	0.0	0	0.0
Balanoposthitis (10004078)	2	1	1	100	0	0.0	0	0.0	0	0.0
Bronchiolitis (10006448)	1	45	45	100	0	0.0	0	0.0	0	0.0
	2	33	33	100	0	0.0	0	0.0	0	0.0
Bronchitis (10006451)	1	6	6	100	0	0.0	0	0.0	0	0.0
	2	6	6	100	0	0.0	0	0.0	0	0.0
Cellulitis (10007882)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Colitis (10009887)	1	2	2	100	0	0.0	0	0.0	0	0.0
Conjunctivitis (10010741)	1	5	5	100	0	0.0	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0	0	0.0
Conjunctivitis allergic (10010744)	1	1	1	100	0	0.0	0	0.0	0	0.0

			Recovered /Resolved		Recovering /Resolving		Not recovered / not resolved		Recovered / Resolved with sequelqe	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Cough (10011224)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	4	4	100	0	0.0	0	0.0	0	0.0
Croup infectious (10011416)	2	1	1	100	0	0.0	0	0.0	0	0.0
Cystitis (10011781)	2	1	1	100	0	0.0	0	0.0	0	0.0
Dermatitis atopic (10012438)	1	23	23	100	0	0.0	0	0.0	0	0.0
	2	14	14	100	0	0.0	0	0.0	0	0.0
Dermatitis contact (10012442)	2	2	2	100	0	0.0	0	0.0	0	0.0
Dermatitis diaper (10012444)	2	6	6	100	0	0.0	0	0.0	0	0.0
Dyspepsia (10013946)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0	0	0.0
Ear infection (10014011)	1	1	1	100	0	0.0	0	0.0	0	0.0
Eczema (10014184)	1	2	2	100	0	0.0	0	0.0	0	0.0
Empyema (10014568)	1	2	2	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Enteritis infectious (10058839)	2	1	1	100	0	0.0	0	0.0	0	0.0
Entropion (10061842)	2	1	1	100	0	0.0	0	0.0	0	0.0
Eye discharge (10015915)	1	2	2	100	0	0.0	0	0.0	0	0.0
Fungal infection (10017533)	2	1	1	100	0	0.0	0	0.0	0	0.0
Gastritis (10017853)	1	6	6	100	0	0.0	0	0.0	0	0.0
	2	4	4	100	0	0.0	0	0.0	0	0.0
Gastroenteritis (10017888)	1	22	22	100	0	0.0	0	0.0	0	0.0
	2	7	7	100	0	0.0	0	0.0	0	0.0
Gastroenteritis viral (10017918)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Gastrointestinal disorder (10017944)	1	19	19	100	0	0.0	0	0.0	0	0.0
	2	8	8	100	0	0.0	0	0.0	0	0.0
Gastrooesophageal reflux disease (10017885)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Hypersensitivity (10020751)	2	2	2	100	0	0.0	0	0.0	0	0.0
Ileus paralytic (10021333)	1	1	1	100	0	0.0	0	0.0	0	0.0
Influenza (10022000)	2	1	1	100	0	0.0	0	0.0	0	0.0

			Recovered /Resolved		Recovering /Resolving		Not recovered / not resolved		Recovered / Resolved with sequelqe	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Jaundice neonatal (10023138)	2	1	1	100	0	0.0	0	0.0	0	0.0
Laryngitis (10023874)	2	1	1	100	0	0.0	0	0.0	0	0.0
Lower respiratory tract infection (10024968)	1	2	2	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Milk allergy (10027633)	1	1	1	100	0	0.0	0	0.0	0	0.0
Nasal congestion (10028735)	1	3	3	100	0	0.0	0	0.0	0	0.0
Nasopharyngitis (10028810)	1	39	39	100	0	0.0	0	0.0	0	0.0
	2	60	59	98.3	0	0.0	0	0.0	1	1.7
Oral candidiasis (10030963)	1	4	4	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Otitis externa (10033072)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Otitis media (10033078)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	6	6	100	0	0.0	0	0.0	0	0.0
Otitis media acute (10033079)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	5	4	80.0	0	0.0	0	0.0	1	20.0
Pharyngitis (10034835)	1	9	9	100	0	0.0	0	0.0	0	0.0
	2	4	4	100	0	0.0	0	0.0	0	0.0
Pneumonia (10035664)	1	3	3	100	0	0.0	0	0.0	0	0.0
Rash (10037844)	1	1	1	100	0	0.0	0	0.0	0	0.0
Regurgitation (10067171)	1	1	1	100	0	0.0	0	0.0	0	0.0
Respiratory tract infection (10062352)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0
Rhinitis (10039083)	1	5	5	100	0	0.0	0	0.0	0	0.0
	2	7	7	100	0	0.0	0	0.0	0	0.0
Rhinorrhoea (10039101)	1	1	1	100	0	0.0	0	0.0	0	0.0
Seborrhoeic dermatitis (10039793)	1	3	3	100	0	0.0	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0	0	0.0
Sepsis (10040047)	1	1	1	100	0	0.0	0	0.0	0	0.0
Skin lesion (10040882)	2	1	1	100	0	0.0	0	0.0	0	0.0
Tonsillitis (10044008)	1	1	1	100	0	0.0	0	0.0	0	0.0
	2	1	1	100	0	0.0	0	0.0	0	0.0

			Recovered /Resolved		Recovering /Resolving		Not recovered / not resolved		Recovered / Resolved with sequelqe	
Preferred Term (Code)	**Dose**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Tremor (10044565)	2	1	1	100	0	0.0	0	0.0	0	0.0
Tubulointerstitial nephritis (10048302)	2	1	1	100	0	0.0	0	0.0	0	0.0
Ulcer (10045285)	2	1	1	100	0	0.0	0	0.0	0	0.0
Upper respiratory tract infection (10046306)	1	12	12	100	0	0.0	0	0.0	0	0.0
	2	13	13	100	0	0.0	0	0.0	0	0.0
Urethritis (10046480)	1	1	1	100	0	0.0	0	0.0	0	0.0
Urinary tract infection (10046571)	1	1	1	100	0	0.0	0	0.0	0	0.0
Urticaria (10046735)	1	2	2	100	0	0.0	0	0.0	0	0.0
	2	2	2	100	0	0.0	0	0.0	0	0.0

N = Number of events
n (%) = number (percentage)of events with the specified category
* The classification of adverse events as expected & unexpected AEs was done by low level term code mentioned in the cleaning report of this study.

VI. Line Listings of adverse events

6. Line-listing of Adverse Events

Line-listing of adverse drug reactions [Appendix No. 3-1]

Line-listing of serious adverse events, adverse drug reaction in PMS special surveillance and post-marketing clinical trial [Appendix No. 3-2]

Line-listing of adverse events [Appendix No.4]

Table of adverse events [Appendix No. 5]

Individual line-listing [Appendix No.7]: provided separately

[Annex 3-1] Line-listing of adverse drug reactions

Incidence of related symptoms during the entire study period.

Time Target	Before licence	Case report 1st & 2nd year
Study institute (A) *No of sites*	-	35
Subject included in the safety analysis Group(B)	-	876
Subject with observed AE (C) *No of subject who report ANY AEs*	-	118
Symptom reported as AE(D) *No of reported AEs*	-	195
Incidence of AE(C/B)	-	13.47%

		# of subjects who experienced the corresponding adverse events (%)[#of events]
		Year 1 & 2
System organ class (code)	**Preferred Term (code)**	**n (%) [n*]**
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	15(1.7)[16]
	Gastrointestinal disorder (10017944)	3(0.3)[3]
	Vomiting (10047700)	44(5.0)[45]
General disorders and administration site conditions (10018065)	Irritability (10022998)	47(5.4)[53]
	Pyrexia (10037660)	27(3.1)[29]
Immune system disorders (10021428)	Hypersensitivity (10020751)	1(0.1)[1]
Infections and infestations (10021881)	Bronchiolitis (10006448)	2(0.2)[2]
	Gastroenteritis (10017888)	1(0.1)[1]
	Otitis media (10033078)	1(0.1)[1]
	Upper respiratory tract infection (10046306)	5(0.6)[5]
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	26(3.0)[26]
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	10(1.1)[11]

		# of subjects who experienced the corresponding adverse events (%)[#of events]
		Year 1 & 2
System organ class (code)	**Preferred Term (code)**	**n (%) [n*]**
Skin and subcutaneous tissue disorders (10040785)	Dermatitis atopic (10012438)	1(0.1)[1]
	Urticaria (10046735)	1(0.1)[1]

[Annex 3-2] Line-listing of serious adverse events, adverse drug reaction in PMS and special surveillance and post-marketing clinical trial

Time Target	Before licence	Case report 1st & 2nd year
Study institute (A) *No of sites*	-	35
Subject included in the safety analysis Group(B)	-	876
Subject with observed AE (C) *No of subject who report ANY AEs*	-	124
Symptom reported as AE(D) *No of reported AEs*	-	206
Incidence of AE(C/B)	-	14.15%

		# of subjects who experienced the corresponding adverse events (%)[#of events]
		Year 1 & 2
System organ class (code)	**Preferred Term (code)**	**n (%) [n*]**
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	15(1.7)[16]
	Gastrointestinal disorder (10017944)	3(0.3)[3]
	Vomiting (10047700)	44(5.0)[45]
	Ileus paralytic (10021333)	1(0.1)[1]
General disorders and administration site conditions (10018065)	Irritability (10022998)	47(5.4)[53]
	Pyrexia (10037660)	27(3.1)[29]
Immune system disorders (10021428)	Hypersensitivity (10020751)	1(0.1)[1]
Infections and infestations (10021881)	Bronchiolitis (10006448)	6(0.7)[6]
	Gastroenteritis (10017888)	3(0.3)[3]
	Otitis media (10033078)	1(0.1)[1]
	Otitis media acute (10033079)	2((0.2)[2]
	Upper respiratory tract infection (10046306)	5(0.6)[5]
	Croup infectious (10011416)	1(0.1)[1]
	Sepsis(10040047)	1(0.1)[1]
Metabolism and nutrition disorders	Decreased appetite (10061428)	26(3.0)[26]

		# of subjects who experienced the corresponding adverse events (%)[#of events]
		Year 1 & 2
System organ class (code)	**Preferred Term (code)**	**n (%) [n*]**
(10027433)		
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	10(1.1)[11]
Skin and subcutaneous tissue disorders (10040785)	Dermatitis atopic (10012438)	1(0.1)[1]
	Urticaria (10046735)	1(0.1)[1]
other		

[Annex4] Line listing of AEs

Incidence of adverse events reported during the entire study period.

Target	Before licence	Case report
		1st & 2nd year
Study institute (A) No of sites	-	35
Subject included in the safety analysis Group (B)	-	876
Subject with observed AE (C) No of subject who report ANY AEs	-	630
Symptom reported as AE (D) No of reported AEs	-	2010
Incidence of AE (C/B)	-	71.91%

		# of subjects who experienced the corresponding adverse events (%)[#of events]
		Year 1 & 2
System organ class (code)	Preferred Term (Code)	n (%) [n*]
Eye disorders (10015919)	Conjunctivitis (10010741)	7(0.8)[7]
	Conjunctivitis allergic (10010744)	1(0.1)[1]
	Entropion (10061842)	1(0.1)[1]
	Eye discharge (10015915)	2(0.2)[2]
Gastrointestinal disorders (10017947)	Colitis (10009887)	2(0.2)[2]
	Constipation (10010774)	5(0.6)[5]
	Diarrhoea (10012735)	55(6.3)[56]
	Dyspepsia (10013946)	3(0.3)[3]
	Gastritis (10017853)	8(0.9)[10]
	Gastrointestinal disorder (10017944)	26(3.0)[27]
	Gastrooesophageal reflux disease (10017885)	2(0.2)[2]
	Ileus paralytic (10021333)	1(0.1)[1]
	Regurgitation (10067171)	1(0.1)[1]
	Vomiting (10047700)	200(22.8)[224]
General disorders and administration site conditions (10018065)	Irritability (10022998)	405(46.2)[488]
	Pyrexia (10037660)	138(15.8)[150]
	Ulcer (10045285)	1(0.1)[1]
Immune system disorders (10021428)	Atopy (10003645)	6(0.7)[6]
	Hypersensitivity (10020751)	2(0.2)[2]

		# of subjects who experienced the corresponding adverse events (%)[#of events]
		Year 1 & 2
System organ class (code)	Preferred Term (Code)	n (%) [n*]
	Milk allergy (10027633)	1(0.1)[1]
Infections and infestations (10021881)	Acute sinusitis (10001076)	3(0.3)[3]
	Acute tonsillitis (10001093)	4(0.5)[4]
	Bronchiolitis (10006448)	65(7.4)[79]
	Bronchitis (10006451)	12(1.4)[12]
	Cellulitis (10007882)	2(0.2)[2]
	Croup infectious (10011416)	1(0.1)[1]
	Cystitis (10011781)	1(0.1)[1]
	Ear infection (10014011)	1(0.1)[1]
	Empyema (10014568)	3(0.3)[3]
	Enteritis infectious (10058839)	1(0.1)[1]
	Fungal infection (10017533)	1(0.1)[1]
	Gastroenteritis (10017888)	24(2.7)[29]
	Gastroenteritis viral (10017918)	2(0.2)[2]
	Influenza (10022000)	1(0.1)[1]
	Laryngitis (10023874)	1(0.1)[1]
	Lower respiratory tract infection (10024968)	2(0.2)[3]
	Nasopharyngitis (10028810)	79(9.0)[99]
	Oral candidiasis (10030963)	4(0.5)[5]
	Otitis externa (10033072)	2(0.2)[2]
	Otitis media (10033078)	7(0.8)[7]
	Otitis media acute (10033079)	7(0.8)[8]
	Pharyngitis (10034835)	11(1.3)[14]
	Pneumonia (10035664)	3(0.3)[3]
	Respiratory tract infection (10062352)	2(0.2)[4]
	Rhinitis (10039083)	8(0.9)[12]
	Sepsis (10040047)	1(0.1)[1]
	Tonsillitis (10044008)	1(0.1)[2]
	Upper respiratory tract infection (10046306)	80(9.1)[90]
	Urethritis (10046480)	1(0.1)[1]
	Urinary tract infection (10046571)	1(0.1)[1]
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	259(29.6)[296]
Nervous system disorders (10029205)	Tremor (10044565)	1(0.1)[1]
Pregnancy, puerperium and perinatal conditions (10036585)	Jaundice neonatal (10023138)	1(0.1)[1]
Renal and urinary disorders (10038359)	Tubulointerstitial nephritis (10048302)	1(0.1)[1]
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	1(0.1)[1]
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	2(0.2)[2]
	Cough (10011224)	209(23.9)[243]

		# of subjects who experienced the corresponding adverse events (%)[#of events]
		Year 1 & 2
System organ class (code)	**Preferred Term (Code)**	**n (%) [n*]**
	Nasal congestion (10028735)	3(0.3)[3]
	Rhinorrhoea (10039101)	7(0.8)[7]
Skin and subcutaneous tissue disorders (10040785)	Dermatitis (10012431)	12(1.4)[12]
	Dermatitis atopic (10012438)	34(3.9)[37]
	Dermatitis contact (10012442)	2(0.2)[2]
	Dermatitis diaper (10012444)	6(0.7)[6]
	Eczema (10014184)	2(0.2)[2]
	Rash (10037844)	3(0.3)[3]
	Seborrhoeic dermatitis (10039793)	4(0.5)[5]
	Skin lesion (10040882)	1(0.1)[1]
	Urticaria (10046735)	4(0.5)[4]

Note: subjects No.PPD reported ACUTE BRONCHIOLITIS , and Subject No PPD reported ACUTE PHARYNGITIS 31 days after Dose 1. So these two AEs are counted in the above table.

[Annex No.5] Table of adverse event

[Annex No. 6] List of license in other countries

Country where the drug is marketed	Effective date and additional action date (Approval date)	Marketing date	Product Name	Remarks
Albania	20-Nov-08		Rotarix	Rota-lyophilised
Argentina	27-Dec-05	06-Jan-06	Rotarix	Rota-lyophilised
Aruba	30-Nov-05		Rotarix	Rota-lyophilised
Australia	08-Mar-06	23-May-06	Rotarix	Rota-lyophilised
Austria	21-Feb-06	02-May-06	Rotarix	Rota-lyophilised
Azerbajian	01-Dec-08	01-Mar-09	Rotarix	Rota-lyophilised
Bahrain	12-Jul-05	12-Oct-05	Rotarix	Rota-lyophilised
Bangladesh	28-Dec-06	28-Mar-07	Rotarix	Rota-lyophilised
Belarus	28-Jun-08		Rotarix	Rota-lyophilised
Belgium	21-Feb-06	01-Jun-06	Rotarix	Rota-lyophilised
Benin	15-Jan-07	15-Apr-07	Rotarix	Rota-lyophilised
Bolivia	12-Dec-06		Rotarix	Rota-lyophilised
Brazil	11-Jul-05	01-Aug-05	Rotarix	Rota-lyophilised
Bulgaria	21-Feb-06	21-May-06	Rotarix	Rota-lyophilised
Burkina Faso	13-Sep-06	13-Dec-06	Rotarix	Rota-lyophilised
Cambodia	39682	22-Nov-08	Rotarix	Rota-lyophilised
Cameroon	24-Aug-05	24-Nov-05	Rotarix	Rota-lyophilised
Canada	09-Oct-07	09-Jan-08	Rotarix	Rota-lyophilised
Chile	18-Aug-05	07-Mar-06	Rotarix	Rota-lyophilised
Colombia	09-Aug-05	10-Sep-05	Rotarix	Rota-lyophilised
Congo	23-Aug-05	23-Nov-05	Rotarix	Rota-lyophilised
Costa Rica	03-Nov-06	28-Feb-07	Rotarix	Rota-lyophilised
Croatia	26-Jun-08	26-Sep-08	Rotarix	Rota-lyophilised
Curacao	06-Sep-05		Rotarix	Rota-lyophilised
Cyprus	21-Feb-06	20-Oct-07	Rotarix	Rota-lyophilised
Czech Republic	21-Feb-06	01-Dec-06	Rotarix	Rota-lyophilised
Democratic Republic of Congo	18-Aug-05		Rotarix	Rota-lyophilised
Denmark	21-Feb-06	17-Jul-06	Rotarix	Rota-lyophilised
Dominican Republic	04-Jun-04	16-Feb-06	Rotarix	Rota-lyophilised
Ecuador	21-Oct-05	31-Jan-06	Rotarix	Rota-lyophilised
Egypt	05-Apr-07	30-Jun-07	Rotarix	Rota-lyophilised
El Salvador	31-Aug-05	10-Oct-05	Rotarix	Rota-lyophilised
Estonia	21-Feb-06	11-Sep-06	Rotarix	Rota-lyophilised
Finland	21-Feb-06	15-May-06	Rotarix	Rota-lyophilised

France	21-Feb-06	29-May-06	Rotarix	Rota-lyophilised
Gabon	31-Mar-05	01-Jul-05	Rotarix	Rota-lyophilised
Germany	21-Feb-06	28-Apr-06	Rotarix	Rota-lyophilised
Greece	21-Feb-06	16-Nov-06	Rotarix	Rota-lyophilised
Guatemala	06-Jun-05	20-Jul-05	Rotarix	Rota-lyophilised
Guinea	09-Feb-06		Rotarix	Rota-lyophilised
Honduras	31-May-06	31-Aug-06	Rotarix	Rota-lyophilised
Hong Kong	21-Jul-06		Rotarix	Rota-lyophilised
Hungary	21-Feb-06	01-Oct-06	Rotarix	Rota-lyophilised
Iceland	24-Apr-06		Rotarix	Rota-lyophilised
India	21-Feb-08	21-May-08	Rotarix	Rota-lyophilised
Ireland	21-Feb-06	01-Mar-07	Rotarix	Rota-lyophilised
Israel	23-Oct-07	23-Jan-08	Rotarix	Rota-lyophilised
Italy	21-Feb-06	24-Oct-06	Rotarix	Rota-lyophilised
Ivory Coast	21-Dec-06	21-Mar-07	Rotarix	Rota-lyophilised
Jamaica	23-Nov-05	19-Feb-06	Rotarix	Rota-lyophilised
Jordan	05-Mar-07	05-Jun-07	Rotarix	Rota-lyophilised
Kazakhstan	04-Jul-07		Rotarix	Rota-lyophilised
Kenya	13-Jul-05	30-Apr-06	Rotarix	Rota-lyophilised
Kuwait	25-Dec-07	25-Mar-08	Rotarix	Rota-lyophilised
Latvia	21-Feb-06	08-Aug-08	Rotarix	Rota-lyophilised
Lebanon	30-Apr-08	30-Jul-08	Rotarix	Rota-lyophilised
Lithuania	21-Feb-06	13-Jul-06	Rotarix	Rota-lyophilised
Luxembourg	21-Feb-06	21-May-06	Rotarix	Rota-lyophilised
Madagascar	20-Dec-05		Rotarix	Rota-lyophilised
Malawi	18-Apr-05		Rotarix	Rota-lyophilised
Malaysia	23-Mar-06	23-Jun-06	Rotarix	Rota-lyophilised
Mali	26-Jan-06	26-Apr-06	Rotarix	Rota-lyophilised
Malta	21-Feb-06	01-Jul-06	Rotarix	Rota-lyophilised
Mauritania	18-May-06		Rotarix	Rota-lyophilised
Mauritius	26-Apr-05	25-Mar-06	Rotarix	Rota-lyophilised
Mexico	12-Jul-04	20-Dec-04	Rotarix	Rota-lyophilised
Morocco	16-Aug-06	16-Nov-06	Rotarix	Rota-lyophilised
Myanmar	29-May-07	29-Aug-07	Rotarix	Rota-lyophilised
Namibia	38905	07-Oct-06	Rotarix	Rota-lyophilised
Netherlands	21-Feb-06	29-Jun-06	Rotarix	Rota-lyophilised
New Zealand	21-Dec-06	21-Mar-07	Rotarix	Rota-lyophilised
Nicaragua	24-Apr-06	24-Jul-06	Rotarix	Rota-lyophilised
Niger	17-Jul-07		Rotarix	Rota-lyophilised
Nigeria	31-Jan-06	01-May-06	Rotarix	Rota-lyophilised

Norway	08-Mar-06	10-Jun-06	Rotarix	Rota-lyophilised
Pakistan	25-Jan-07	25-Apr-07	Rotarix	Rota-lyophilised
Panama	22-Dec-05	08-Mar-06	Rotarix	Rota-lyophilised
Paraguay	16-Aug-06	16-Nov-06	Rotarix	Rota-lyophilised
Peru	26-Jul-05	18-Aug-05	Rotarix	Rota-lyophilised
Philippines	01-Sep-05	01-Dec-05	Rotarix	Rota-lyophilised
Poland	21-Feb-06	06-Jul-06	Rotarix	Rota-lyophilised
Portugal	21-Feb-06	29-May-06	Rotarix	Rota-lyophilised
Qatar	24-May-06	30-Nov-06	Rotarix	Rota-lyophilised
RCA	04-Oct-05		Rotarix	Rota-lyophilised
Romania	21-Feb-06	21-May-06	Rotarix	Rota-lyophilised
Saudi Arabia	30-May-06	30-Aug-06	Rotarix	Rota-lyophilised
Senegal	21-Apr-06	21-Jul-06	Rotarix	Rota-lyophilised
Serbia	02-Oct-08		Rotarix	Rota-lyophilised
Singapore	05-Oct-05	20-Oct-05	Rotarix	Rota-lyophilised
Slovakia	21-Feb-06	23-Oct-06	Rotarix	Rota-lyophilised
Slovenia	21-Feb-06	05-Jan-07	Rotarix	Rota-lyophilised
South Africa	07-Jul-06	07-Oct-06	Rotarix	Rota-lyophilised
South Korea	07-Mar-08	Jun-08	Rotarix	Rota-lyophilised
Spain	21-Feb-06	24-Jul-06	Rotarix	Rota-lyophilised
Sri Lanka	26-May-06	26-Aug-06	Rotarix	Rota-lyophilised
Suriname	05-May-05		Rotarix	Rota-lyophilised
Sweden	21-Feb-06	15-Jun-06	Rotarix	Rota-lyophilised
Switzerland	29-Jan-07	30-Apr-07	Rotarix	Rota-lyophilised
Taiwan	31-Aug-06	01-Dec-06	Rotarix	Rota-lyophilised
Thailand	30-Dec-05	31-Mar-06	Rotarix	Rota-lyophilised
Togo	02-Jun-06	02-Sep-06	Rotarix	Rota-lyophilised
Trinidad and Tobago	05-Jul-05	21-Sep-05	Rotarix	Rota-lyophilised
Tunisia	08-Mar-08	08-Jun-08	Rotarix	Rota-lyophilised
Uganda	14-Aug-09		Rotarix	Rota-lyophilised
UK	21-Feb-06	22-May-06	Rotarix	Rota-lyophilised
United Arab Emirates	28-Nov-05	23-Mar-06	Rotarix	Rota-lyophilised
United States	03-Apr-08	03-Jul-08	Rotarix	Rota-lyophilised
Venezuela	22-Sep-05	21-Jan-06	Rotarix	Rota-lyophilised
Vietnam	28-May-07	29-Jul-07	Rotarix	Rota-lyophilised
WHO	30-Jan-07	30-Apr-07	Rotarix	Rota-lyophilised
Yemen	31-Jul-06	31-Oct-06	Rotarix	Rota-lyophilised
Argentina	02-Feb-09	02-Dec-09	Rotarix	Rota-Liquid
Australia	08-Aug-08	01-Mar-09	Rotarix	Rota-Liquid

Austria	01-Sep-08		Rotarix	Rota-Liquid
Bangladesh	28-Jan-10		Rotarix	Rota-Liquid
Belgium	01-Sep-08		Rotarix	Rota-Liquid
Benin	25-May-09		Rotarix	Rota-Liquid
Bolivia	24-Aug-09	01-Oct-09	Rotarix	Rota-Liquid
Brazil	12-Mar-07	19-Sep-07	Rotarix	Rota-Liquid
Bulgaria	01-Sep-08		Rotarix	Rota-Liquid
Burkina Faso	29-Jul-09		Rotarix	Rota-Liquid
Canada	11-Jan-10		Rotarix	Rota-Liquid
Chile	04-Nov-09	04-Feb-10	Rotarix	Rota-Liquid
Colombia	09-Sep-08	01-Sep-09	Rotarix	Rota-Liquid
Congo	30-Jun-09		Rotarix	Rota-Liquid
Cyprus	01-Sep-08		Rotarix	Rota-Liquid
Czech Republic	01-Sep-08		Rotarix	Rota-Liquid
Democratic Republic of Congo	04-Sep-09		Rotarix	Rota-Liquid
Denmark	01-Sep-08		Rotarix	Rota-Liquid
Dominican Republic	03-Jul-09		Rotarix	Rota-Liquid
Ecuador	20-Nov-09	01-Oct-09	Rotarix	Rota-Liquid
El Salvador	26-Mar-09	01-Oct-09	Rotarix	Rota-Liquid
Estonia	01-Sep-08		Rotarix	Rota-Liquid
Finland	01-Sep-08		Rotarix	Rota-Liquid
France	01-Sep-08		Rotarix	Rota-Liquid
Gabon	39994		Rotarix	Rota-Liquid
Germany	01-Sep-08		Rotarix	Rota-Liquid
Greece	01-Sep-08		Rotarix	Rota-Liquid
Guatemala	22-Apr-09		Rotarix	Rota-Liquid
Honduras	25-May-09	01-Sep-09	Rotarix	Rota-Liquid
Hong Kong	20-May-08	28-Sep-08	Rotarix	Rota-Liquid
Hungary	01-Sep-08		Rotarix	Rota-Liquid
Iceland	39692		Rotarix	Rota-Liquid
Ireland	01-Sep-08		Rotarix	Rota-Liquid
Italy	01-Sep-08		Rotarix	Rota-Liquid
Ivory Coast	05-Nov-09		Rotarix	Rota-Liquid
Kenya	01-Aug-08		Rotarix	Rota-Liquid
Latvia	01-Sep-08		Rotarix	Rota-Liquid
Lithuania	01-Sep-08		Rotarix	Rota-Liquid
Luxembourg	01-Sep-08		Rotarix	Rota-Liquid
Malaysia	19-Feb-09		Rotarix	Rota-Liquid

Mali	09-Nov-09		Rotarix	Rota-Liquid
Malta	01-Sep-08		Rotarix	Rota-Liquid
Mexico	10-Jun-09	10-Sep-09	Rotarix	Rota-Liquid
Moldova	06-Feb-09		Rotarix	Rota-Liquid
Myanmar	14-Dec-09		Rotarix	Rota-Liquid
Netherlands	01-Sep-08		Rotarix	Rota-Liquid
New Zealand	27-Mar-09		Rotarix	Rota-Liquid
Nicaragua	18-Jun-09		Rotarix	Rota-Liquid
Niger	05-Jun-09		Rotarix	Rota-Liquid
Norway	39727		Rotarix	Rota-Liquid
Paraguay	20-Jul-09	01-Oct-09	Rotarix	Rota-Liquid
Peru	29-May-09	29-Aug-09	Rotarix	Rota-Liquid
Philippines	16-Feb-09		Rotarix	Rota-Liquid
Poland	01-Sep-08		Rotarix	Rota-Liquid
Portugal	01-Sep-08	23-Apr-09	Rotarix	Rota-Liquid
RCA	04-Jun-09		Rotarix	Rota-Liquid
Romania	01-Sep-08		Rotarix	Rota-Liquid
Singapore	04-Dec-09		Rotarix	Rota-Liquid
Slovakia	01-Sep-08		Rotarix	Rota-Liquid
Slovenia	01-Sep-08	16-Sep-09	Rotarix	Rota-Liquid
South Africa	05-Mar-09	01-Apr-09	Rotarix	Rota-Liquid
Spain	01-Sep-08	06-May-09	Rotarix	Rota-Liquid
Sweden	01-Sep-08		Rotarix	Rota-Liquid
Switzerland	14-May-09		Rotarix	Rota-Liquid
Taiwan	17-Dec-09		Rotarix	Rota-Liquid
Thailand	26-Jun-09		Rotarix	Rota-Liquid
UK	01-Sep-08		Rotarix	Rota-Liquid
Ukraine	10-Jun-09		Rotarix	Rota-Liquid
Uruguay	17-Nov-09	17-Feb-10	Rotarix	Rota-Liquid
Venezuela	10-Feb-09	01-Sep-09	Rotarix	Rota-Liquid
WHO	12-Mar-09		Rotarix	Rota-Liquid

VII. Considerations of the results and future plan

7. Considerations of the results and future plan

This study report presents the data from the surveillance following the registration of Rotarix™ in Korea on 07 March 2008. The safety of GSK Biologicals' Rotarix ™ vaccine was to be assessed in subjects aged 6 – 16 weeks, as per the requirement of Korean Food and Drug Administration.

A total of 877 subjects were enrolled in the surveillance study to receive Rotarix™ vaccine and the safety data collected for 876 subjects were analysed.

- Irritability was the most frequently reported expected AE during the study period. This is in line with other studies conducted in Asia (Bangladesh (Rota-045 trial) [Zaman, 2009] and Japan (Rota-056 trial) (107625\444563)). Majority of the irritability cases lasted for a day after both doses of the study vaccination. Less than 1% of the irritability cases reported after both doses of the study vaccination were assessed by the investigator to be definitely related to vaccination. The severity of irritability cases decreased from post Dose 1 of the study vaccination to post Dose 2 of the study vaccination (7.4% of the irritability cases reported post Dose 1 of the study vaccination and 3.6% of the irritability cases reported post Dose 2 of the study vaccination were assessed as severe).

- Cough was the most frequently reported unexpected AE during the study period. Majority of the cough cases lasted for a day after Dose 1 of the study vaccination and 4 to 7 days after Dose 2 of the study vaccination. None of the cases of cough reported were assessed by the investigator to be definitely related to vaccination. The percentage of cough cases assessed by the investigator to be possibly related to study vaccination was 2.6% post Dose 1 of the study vaccination and 1.1% post Dose 2 of the study vaccination. The percentage of cough cases which were assessed by the investigator to be severe post Dose 1 and Dose 2 of the study vaccination were 0.7% and 1.1%, respectively.

- Irritability, reported for 5.4% of subjects and cough, reported for 1.1% of subjects were also the most frequently reported expected and unexpected ADRs, respectively.

- Of the 118 subjects who had a previous medical history, a total of 85 (72.0%) subjects experienced AEs.

- Overall, at least one expected AE was reported for 62.7% of the subjects who had a previous medical history, 66.0% of subjects who received concomitant medication and 58.3% of the subjects who received concomitant vaccination, respectively. Irritability was the most frequently reported expected AE among subjects who had a previous medical history, subjects who received concomitant medication and subjects who received concomitant vaccination.

- Overall, at least one unexpected AE was reported for 43.2% of the subjects who had a previous medical history, 82.9% of the subjects who received concomitant medication and 46.7% of subjects who received concomitant vaccination, respectively. Cough was the most frequently reported unexpected AE among subjects who had previous medical

history, subjects who received concomitant medication and subjects who received concomitant vaccination.

- Eleven SAEs were reported for 6 subjects during the study period. These included sepsis, bronchiolitis, AOM, acute GE, acute bronchiolitis, paralytic ileus and infectious croup. None of the SAEs were considered by the investigator to have a causal relationship to vaccination.

Thus, the results of this surveillance indicate that GSK Biologicals' live attenuated HRV vaccine, Rotarix™ is well tolerated and has a good safety profile when administered in Korean infants.

References

Zaman K, Sack DA, Yunus M, et al. Successful co-administration of a human rotavirus and oral poliovirus vaccines in Bangladeshi infants in a 2-dose schedule at 12 and 16 weeks of age. Vaccine. 2009; 27(9):1333-9.

VIII. INVOICE SALES

8. Invoice Sales

Period	Shipping amount (60T)

IX. Data on foreign adverse events

9. Data on foreign adverse events

Sponsor:
GlaxoSmithKline Biologicals
9th Floor LS Yongsan Tower building,
191 Hangang-ro-2-ga, Yongsan-gu,
Seoul, 140-702, Korea

Product Names	GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** **(Amendment 4: 23 February 2012)**
eTrack number and abbreviated title	111700 (Rota-070 PMS)
Date of protocol	Final: 11 April 2008
Amendment 1	Final: 09 May 2008
Amendment 2	Final: 13 October 2008
Amendment 3	Final: 10 February 2010
Amendment 4	Final: 23 February 2012
Title	Safety of GlaxoSmithKline Biologicals' oral live attenuated human rotavirus vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea. **(Amendment 4: 23 February 2012)**
Detailed Title	Open, multi-centric, post-marketing surveillance (PMS) to monitor the safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea. **(Amendment 4: 23 February 2012)**
Co-ordinating author	PPD Scientific Writer
Contributing authors	• PPD Bio Medical Director, Korea • PPD Medical Director, Clinical R&D and Medical Affairs, Korea • PPD Senior Manager, GCRD, Rotavirus vaccine

Continued on the next page

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GSK Biologicals' Protocol DS V 12.5

Protocol Amendment 4 Sponsor Signatory Approval

eTrack number and abbreviated title	111700 (Rota-070 PMS)
Amendment 4	Final: 23 February 2012
Detailed Title	Open, multi-centric, post-marketing surveillance (PMS) to monitor the safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea. **(Amendment 4: 23 February 2012)**
Sponsor signatory:	Dr. Emilio F. Ledesma, Vice President, Clinical R&D and Medical Affairs, Asia Pacific
Signature:	_____
Date:	_____

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Protocol Amendment 4 Rationale

Amendment number: Amendment 4
Rationale/background for changes: The protocol has been amended to reflect the two new vaccine presentations that have been launched in Korea. The current PMS will thus collect safety information from subjects who have received either Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe).

Protocol Amendment 4 Investigator Agreement

I agree:

- To assume responsibility for the proper conduct of the study at this site.
- To conduct the study in compliance with this protocol, any mutually agreed future protocol amendments, and with any other study conduct procedures provided by GlaxoSmithKline Biologicals (GSK Biologicals).
- To ensure that all persons assisting me with the study are adequately informed about the GSK Biologicals' Rotarix™ and other study-related duties and functions as described in the protocol.
- Not to implement any changes to the protocol without agreement from the sponsor and prior review and written approval from the Institutional Review Board (IRB) or Independent Ethics Committee (IEC) (except where site does not have IRB/IEC according to APPOL and LSOP), except where necessary to eliminate an immediate hazard to the subjects, or where permitted by all applicable regulatory requirements (for example, for administrative aspects of the study).
- That I am thoroughly familiar with the appropriate use of the vaccine, as described in this protocol, and any other information provided by the sponsor, including, but not limited to, the following: the current Investigator's Brochure (IB) or equivalent document, IB supplement (if applicable), prescribing information (in the case of a marketed vaccine).
- That I am aware of, and will comply with, applicable ethical practices and all applicable regulatory requirements.
- That I have been informed that certain regulatory authorities require the sponsor to obtain and supply, as necessary, details about the investigator's ownership interest in the sponsor or the investigational product, and more generally about his/her financial ties with the sponsor. GSK Biologicals will use and disclose the information solely for the purpose of complying with regulatory requirements.

Hence I:

- Agree that GSK Biologicals may disclose any information it has about such ownership interests and financial ties to regulatory authorities.

eTrack number and abbreviated title	111700 (Rota-070 PMS)
Amendment 4	Final: 23 February 2012
Detailed Title	Open, multi-centric, post-marketing surveillance (PMS) to monitor the safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea. **(Amendment 4: 23 February 2012)**
Investigator name:	

Investigator signature: **Date:**

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Synopsis

Detailed Title	Open, multi-centric, post-marketing surveillance (PMS) to monitor the safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea. **(Amendment 4: 23 February 2012)**
Indication/PMS population	Prevention of gastroenteritis (GE) caused by rotavirus (RV) (serotype G1P[8], G3P[8], G4P[8], G9P[8]) in infants from the age of 6 weeks.
Rationale	GSK Biologicals' vaccine, Rotarix™ ***(lyophilised formulation)*** was registered in Korea in March 2008. ***Rotarix™ liquid formulation (oral suspension) was registered in Korea in January 2011 while Rotarix™ liquid formulation (prefilled syringe) was registered in December 2011. Following the vaccine registration***, safety information on the use of ***all the Rotarix™ presentations*** is required as per the regulations of the Korean Food and Drugs Administration (KFDA) in ***at least*** 3000 ***evaluable*** Korean infants. **(Amendment 4: 23 February 2012)**
Objective	To assess the safety of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** in infants when administered according to the prescribing information in Korea. **(Amendment 4: 23 February 2012)**
PMS design	• PMS design: Open-label, non-comparative, multi-centre PMS in Korea. • Vaccination schedule: Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be administered orally as per the prescribing information in Korea. – First vaccination will be given to infants from the age of 6 weeks. – Second vaccination will be given at least 4 weeks after Dose 1. Administration of Dose 2 is preferably given before the age of 16 weeks. Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** should be given before 24 weeks of age. • Control: None.

- Type of PMS: Self-contained.
- Two visits are recommended as follows:
  - Visit 1: Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination, subjects will be allowed to receive concomitant vaccinations.
  - Visit 2: Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination, subjects will be allowed to receive concomitant vaccinations.
- Recording of AEs from Day 0 to Day 30 using the diary card after each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***.
- Recording of serious adverse events (SAEs) during the entire PMS period.
- Duration of the PMS: The intended duration of the PMS, per infant, will be approximately 3 months.
- Data collection: Standardised hard copy case report form (CRF). **(Amendment 4: 23 February 2012)**

Number of subjects

As per the KFDA requirements, safety information from **at least** 3000 evaluable infants are needed ***for this PMS study.*** **(Amendment 4: 23 February 2012)**

Endpoints

- Occurrence of AEs during the 31-day (Day 0 – Day 30) follow-up period after each vaccine dose according to Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of SAEs during the entire PMS period.

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List of Abbreviations

AE	Adverse event
$CCID_{50}$	Median cell culture infective dose (quantity of virus causing infection in 50% of exposed cells)
CI	Confidence Interval
CRF	Case Report Form
GAVI	Global Alliance for Vaccines and Immunisations
GCP	Good Clinical Practice
GE	Gastroenteritis
GSK	GlaxoSmithKline
HRV	Human Rotavirus
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IRB	Institutional Review Board
KFDA	Korean Food and Drugs Administration
MedDRA	Medical Dictionary for Regulatory Activities
PATH	Program for Appropriate Technology in Health
PMS	Post Marketing Surveillance
RV	Rotavirus
SAE	Serious Adverse Events
SOP	Standard Operating Procedure
WHO	World Health Organisation

Glossary of Terms

Adverse event:	Any untoward medical occurrence, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.
Diarrhoea:	Passage of three or more looser than normal stools (loose or watery stools), within a day.
Eligible:	Qualified for enrolment into the PMS based upon strict adherence to inclusion/exclusion criteria.
eTrack:	GSK's clinical trials tracking tool.
Expected adverse event:	The presence/occurrence/intensity of an adverse event that is expected from the infant or an observer during the post-vaccination follow-up period as described in the locally approved prescribing information.
Gastroenteritis:	Diarrhoea with or without vomiting.
Medical Monitor:	An individual medically qualified to assume the responsibilities of the sponsor (GSK Biologicals) especially in regards to the ethics, clinical safety of a PMS and the assessment of adverse events.
Protocol amendment:	ICH defines a protocol amendment as: "A written description of a change(s) to or formal clarification of a protocol." GSK Biologicals further details this to include a change to an approved protocol that affects the safety of subjects, scope of the investigation, PMS design, or scientific integrity of the PMS.
Protocol administrative change:	A protocol administrative change addresses changes to only logistical or administrative aspects of the PMS. N.B. Any change that falls under the definition of a protocol amendment (e.g. a change that affects the safety of subjects, scope of the investigation, PMS design, or scientific integrity of the PMS) MUST be prepared as an amendment to the protocol.

Site Monitor:	An individual assigned by the sponsor who is responsible for assuring proper conduct of the PMS at one or more investigational sites.
Study Monitor:	An individual assigned by the sponsor who is responsible for assuring proper conduct of a PMS.
Subject:	Term used throughout the protocol to denote an individual whose parents/guardians have been contacted in order to participate in the PMS.
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the PMS.
Unexpected adverse event:	Any adverse event that is not reflected in the locally approved prescribing information.
Vomiting:	One or more episodes of forceful emptying of partially digested stomach contents ≥ 1 hour after feeding within a day.

1. INTRODUCTION

Rotavirus (RV) is associated with acute gastroenteritis (GE) in infants and is responsible for approximately half a million deaths in children in developing countries [Glass, 2006; Steele, 2003]. High mortality due to RV is evident in developing countries such as Africa, Latin America and the Asian subcontinent. RV is prevalent in Asia all year around causing about 45% of the diarrhoeal hospitalisations in children less than 5 years of age [Phua, 2006]. Previous studies conducted revealed that RV was responsible for 46% of 4668 hospitalisations among Korean children with acute GE. Also, RV was the most prevalent etiologic agent causing severe diarrhoeal illness among children aged 6-24 months, which accounted for 84% of all cases [Seo, 2000].

The large global health burden due to RV disease in both developed and developing countries prompted the development of RV vaccines since only non-specific symptomatic therapies are available. In fact, in recent years, many international organisations such as World health Organisation (WHO), the Global Alliance for Vaccines and Immunisations (GAVI) and the Children's Vaccine Program at the Program for Appropriate Technology in Health (PATH) have identified RV vaccines as a priority for development. [Fischer, 2007; WHO, 2007; Glass, 2005; Bresse, 2004].

1.1. Background

GSK Biologicals has produced an oral live attenuated human rotavirus (HRV) vaccine [Rotarix™] containing the RIX4414 vaccine strain of G1P1A P[8] specificity developed from the parent 89-12 vaccine strain with proven efficacy [Bernstein, 1998; Bernstein, 1999; Bernstein, 2002].

Rotarix™ has been evaluated in Phase I – III clinical studies in Asia (including Korea), Africa, Europe, Latin America and North America.

Clinical trials conducted with Rotarix™ showed that two doses of the vaccine were immunogenic, well tolerated, and effective against RV GE hospitalisations, severe RV GE and any RV GE caused by several circulating strains [Ruiz-Palacios, 2006; Salinas, 2005; Vesikari, 2006]. In a large phase III clinical trial in Latin America, vaccine efficacy against severe RV GE was 84.7% [95% CI: 71.7%; 92.4%] (p-value <0.001) and vaccine efficacy against serotype-specific (G1P[8]) severe RV GE (with a score of ≥ 11 on the Vesikari scale) was 90.8% [95% CI: 70.5%; 98.2%]. This study also demonstrated that the vaccine was not associated with an increased risk of intussusception during 31 days after administration of either of the two doses as compared to the placebo. The overall serious adverse event (SAE) profile of the vaccine was similar to the placebo [Ruiz-Palacios, 2006].

A phase III trial was conducted in Korea to assess the reactogenicity and immunogenicity profile of the vaccine. Two doses of the vaccine were shown to be well-tolerated, immunogenic (66.7% [95% CI: 51.6%; 79.6%]) with a good safety profile [Jung Soo, 2007].

In a phase III trial conducted in the European Union, the vaccine efficacy during the first efficacy follow-up period (2 weeks post-dose 2 up to the end of the first RV season) was 95.8% [95%CI: 89.6%; 98.7%] against severe RV GE. Vaccine efficacy was 90.4% [95% CI: 85.1%; 94.1%] against severe RV GE in the combined efficacy period (2 weeks post-dose 2 through the two consecutive RV seasons following vaccinations). For increasing disease severity with Vesikari scores between 11 and 20, vaccine efficacy was increasingly higher, reaching 100% against more severe RV GE (Vesikari score ≥ 17 points) The HRV vaccine was highly protective against any and severe RV GE caused by G1, G3, G4 and G9 strains. Vaccine efficacy against severe RV GE caused by G2 serotype was 85.5% [95% CI: 24.0%; 98.5%] in the combined efficacy period [Vesikari, 2007].

Co-administration of routine childhood vaccines with two doses of Rotarix™ elicited excellent vaccine take and were well tolerated in studies conducted in United States, Canada, Singapore, Latin America and Europe [Dennehy, 2005; Phua, 2005; Salinas, 2005; Vesikari, 2006]. The lyophilised formulation of Rotarix™ is currently licensed in over 100 countries worldwide and has been recommended for inclusion in National Immunisation programs in Brazil, Venezuela, Ecuador, Panama, El Salvador, Mexico and Australia.

1.2. Rationale for the Post Marketing Surveillance (PMS)

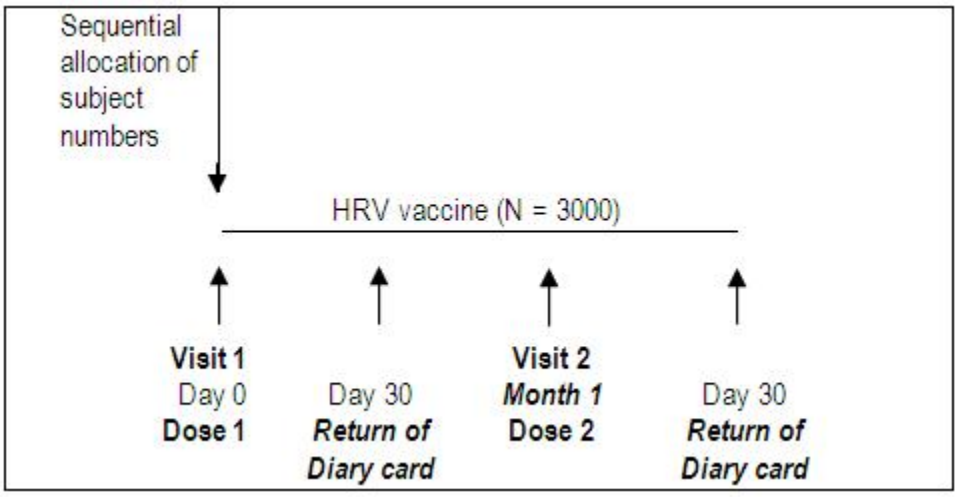
GSK Biologicals' vaccine, Rotarix™ ***(lyophilised formulation)*** was registered in Korea in March 2008. ***Rotarix™ liquid formulation (oral suspension) was registered in Korea in January 2011 while Rotarix™ liquid formulation (prefilled syringe) was registered in December 2011. Following the vaccine registration***, safety information on the use of ***all the Rotarix™ presentations*** is required as per the regulations of the Korean Food and Drugs Administration (KFDA) in ***at least*** 3000 ***evaluable*** Korean infants. **(Amendment 4: 23 February 2012)**

2. OBJECTIVE

To assess the safety of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** in infants when administered according to the prescribing information in Korea. **(Amendment 4: 23 February 2012)**

Refer to Section 10.1 for definition of the endpoints.

3. PMS DESIGN OVERVIEW



N: Number of subjects planned to be enrolled.
Infants who have received a dose of the vaccine prior to the start of the PMS will have only one visit followed by the phone contact.
PMS conclusion: An infant's parent/guardian who will be contacted to provide details of any AEs experienced by the infant 30 days after the infant receives the last vaccination or an infant for whom diary card transcription into CRF will be been done through phone contact is considered to have completed the PMS.

- PMS design: Open-label, non-comparative, multi-centre PMS in Korea.
- Vaccination schedule: Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be administered orally as per the prescribing information in Korea.
  - First vaccination will be given to infants from the age of 6 weeks.
  - Second vaccination will be given at least 4 weeks after Dose 1. Administration of Dose 2 is preferably given before the age of 16 weeks.

  Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** should be given before 24 weeks of age.
- Control: None.
- Type of PMS: Self-contained.
- Two visits are recommended as follows:
  - Visit 1: Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination, subjects will be allowed to receive concomitant vaccinations.
  - Visit 2: Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination, subjects will be allowed to receive concomitant vaccinations.
- Recording of AEs from Day 0 to Day 30 using diary cards after each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***.

- Recording of SAEs during the entire PMS period.
- Duration of the PMS: The intended duration of the PMS, per infant, will be approximately 3 months.
- Refer to Appendix B for details of the recruitment plan.
- Data collection: Standardised hard copy case report form (CRF).

(Amendment 4: 23 February 2012)

4. PMS COHORT

4.1. Number of subjects / centres

As per the KFDA requirements, safety information from at least 3000 evaluable infants are needed ***for this PMS study***.

Infants will be recruited from the age of 6 weeks in this multi-centre PMS.

Details of recruitment at each centre, including any criteria for termination of enrolment at a particular centre, will be discussed in the recruitment plan, which is summarised in Appendix B **(Amendment 4: 23 February 2012)**

4.2. Inclusion criteria

Infants who satisfy the following criteria can enter the PMS:

- Infants who the investigator believes that their parents/guardians can and will comply with the requirements of the protocol (e.g. completion of the diary cards) should be enrolled in the PMS.
- A male or female infant from the age of 6 weeks at the time of the first vaccination. (Note: Two doses of the Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccine should be completed by the age of 24 weeks). **(Amendment 4: 23 February 2012)**
- Written informed consent obtained from the parent or guardian of the infant.

4.3. Exclusion criteria for enrolment

At the time of PMS entry, the contraindications and precautions of use indicated in the prescribing information should be checked and the infant must not be included in the PMS if there is any contraindication. Any changes in the locally approved Prescribing Information must be implemented immediately.

4.4. Elimination criteria during the PMS

Not applicable.

4.5. Contraindications to subsequent vaccination

Refer to the prescribing information for contraindications. Any changes in the locally approved Prescribing Information must be implemented immediately.

4.6. Warnings and Precautions

Refer to the prescribing information for warnings and precautions. Any changes in the locally approved Prescribing Information must be implemented immediately.

5. CONDUCT OF PMS

5.1. Ethics and regulatory considerations

The PMS will be conducted according to the local rules and regulations of the country (KFDA) and relevant GSK SOPs/Policies and Guidance.

Submission of the protocol and any protocol amendments to regulatory agencies will occur in accordance with local regulatory requirements and relevant GSK SOPs/Policies and Guidance. If needed, this protocol/protocol amendment will be submitted to an Institutional Review Board (IRB).

Independent Ethics Committee/Institutional Review Board (IEC/IRB) approval has to be obtained prior to study start. If the regulatory authority and/or IEC/IRB advise that PMS studies do not need ethical review this must be documented. In any event, submission to an IEC/IRB in all institutions where IEC/IRB are available must be carried out and documented.

5.1.1. Informed consent

In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and to the applicable ethical principles. Prior to the beginning of the PMS, the investigator should have, if applicable, the IRB written approval/favourable opinion of the written informed consent form and any other written information to be provided to the participating infants' parents/guardians, if applicable.

Freely given informed consent should be obtained from every infants' parents/guardians for the collection of personal and safety information prior to or post vaccination.

Information should be given in both oral and written form whenever possible and as deemed appropriate by the IRB.

An investigator or designate will describe the protocol to potential infants' parents/guardians face to face. The Informed Consent Form may be read to the infants' parents/guardians, but, in any event, the investigator or designate shall give the infants' parents/guardians ample opportunity to inquire about details of the PMS and ask any questions before dating and signing the Informed Consent Form.

While informed consent information can be presented to groups at an initial information session, each infant's parents/guardians must be given the opportunity to individually pose questions to the investigator or designate prior to the infant's parents/ guardians dating and signing the Informed Consent Form.

Informed Consent Form must be in a language fully comprehensible to the prospective infants' parents/guardians. Informed consent shall be documented by the use of a written consent form (when applicable, approved by the IRB) and signed and dated by the parents/guardians and by the person who conducted the informed consent discussion. The signature confirms the consent is based on information that has been understood. All illiterate individuals will have the PMS, the Informed Consent Form explained to them point by point by the interviewer in the presence of an impartial witness. The witness will personally sign and date the consent form.

Each infant's signed informed consent form must be kept on file by the investigator for possible inspection by Regulatory Authorities and/or GSK Biologicals' professional and Regulatory Compliance persons. The parents/guardians should receive a copy of the signed and dated written informed consent form and any other written information provided to the infants' parents/guardians, and should receive copies of any signed and dated consent form updates. Any amendments to the written information will be provided to infants' parents/guardians.

Both the informed consent discussion and the written informed consent form and any other written information to be provided to the infants' parents/guardians should include explanations of the following:

a. This is a regulatory mandated PMS.

b. The purpose of the PMS.

c. The PMS procedures to be followed.

d. The infant's parents'/guardians' responsibilities.

e. The reasonably foreseeable risks or inconveniences to the infants.

f. The reasonable expected benefits.

g. That the infants' participation in the PMS is voluntary and infants' parents/guardians may refuse to participate or withdraw from the PMS, at any time, without penalty or loss of benefits to which subjects are otherwise entitled.

h. That the monitor(s), the auditor(s), the IRB, and the regulatory authority(ies) will be granted direct access to the infant's original medical records for verification of PMS procedures and/or data, without violating the confidentiality of infant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent, the infant's parents/guardians is authorising such access.

i. That records identifying infants will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the PMS are published, infants' identity will remain confidential.

j. The approximate number of infants involved in the PMS.

k. The expected duration of a infant's participation in the PMS.

GSK Biologicals will prepare a model Informed Consent Form which will embody all the elements described above. While it is strongly recommended that this model document be followed as closely as possible, the informed consent requirements given in this document are not intended to pre-empt any local regulations which require additional information to be disclosed for informed consent to be legally effective. Clinical judgement, local regulations and requirements should guide the final structure and content of the document.

The investigator has the final responsibility for the final presentation of Informed Consent Form, respecting the mandatory requirements of local regulations. The consent form generated by the investigator with the assistance of the sponsor's representative, must be approved (along with the protocol, and any other necessary documentation) by the IRB (if applicable) and be acceptable to GSK Biologicals.

5.2. General PMS aspects

All concomitant vaccinations according to local practice are allowed during the PMS and administration of these should be documented in the CRF.

5.3. Subject identification

Subject numbers will be assigned sequentially to infants whose parents/guardians have given consent to participate in the PMS, according to the range of subject numbers allocated to each PMS centre.

5.4. Outline of PMS procedures

The outline of PMS procedures is presented in Table 1.

Table 1 List of PMS procedures

Age	From the age of 6 weeks			
Visit Timing	VISIT 1 Day 0	Diary Card Return* Day 30 or after	VISIT 2§ At least 4 weeks after Dose 1	Diary Card Return* Day 30 or after
Informed consent	●			
Check inclusion criteria	●			
Check exclusion criteria	●			
Check contraindications	●		●	
Medical history	●			
Physical examination	●		○	
Recording of body temperature	●		●	
Recording of previous Rotarix™ vaccination	●			
Vaccination	●		●	
Recording of AEs occurring from Day 0 to Day 30 after vaccination, by infants' parents/guardians on diary cards	●	●	●	●
Return of diary cards		●		●
Record any concomitant medication/vaccination	●	●	●	●
Reporting of Serious Adverse Events	●	●	●	●
PMS Conclusion		●¶		●

● is used to indicate a PMS procedure that requires documentation in the individual CRF.
○ is used to indicate a PMS procedure that does not require documentation in the individual CRF.
*Diary card will be returned by parents/guardians of infants on Day 30 or after. If the same is not returned, the investigator will make a phone contact to record all AEs in the medical record and then transcribe the information into the CRF.
§Visit 2 will be omitted only for those infants who have received one dose of *Rotarix™* ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** prior to the start of the PMS and have received the second dose of the vaccine at Visit 1 or if the investigator confirms that the infant will not be vaccinated in the same centre. The infants who have received a dose of the vaccine prior to the start of the PMS will have only one visit followed by the phone contact and the post-Dose 2 data collected will be recorded under the Visit 2 section of the CRF.
¶If infants receive the 2nd dose at Visit 1 or if the investigator confirms that infants will not be vaccinated in the same centre. **(Amendment 4: 23 February 2012)**

It is the investigator's responsibility to ensure that the intervals between visits/contacts are followed as closely as possible. There should be an interval of at least 4 weeks between two doses. Administration of the second dose is preferably given before the age of 16 weeks and should be completed by the age of 24 weeks.

However, if circumstances dictate other intervals, this will not lead to the exclusion from the analysis. The date of the previous visit serves as the reference date for intervals between study visits.

5.5. Detailed description of visits

Visit 1 (Day 0): Rotarix™ *or Rotarix™ liquid formulation (oral suspension or prefilled syringe)* vaccination **(Amendment 4: 23 February 2012)**

- Written informed consent obtained from parents/guardians of the infant.
- Checking inclusion/exclusion criteria (See sections 4.2 and 4.3).
- Checking of contraindications to vaccination.
- Recording of medical history and physical examination.
- Recording of body temperature (measured by oral/axillary/tympanic route).
- Record previous history of any Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccine administration (if applicable)
- Vaccination:
  - One dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be administered orally according to instructions specified in section 6.2.
  - Infants will be allowed to receive concomitant vaccinations.

  The vaccinees will be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.
- Diary cards will be provided to the parents/guardians of all infants to record information on AEs occurring on the day of Dose 1 and the following 30 days.

  The infants' parents/guardians will be instructed to contact the investigator immediately should the infant manifest any signs or symptoms they perceive as serious. The parents/guardians should be instructed to return the completed diary card to the investigator 30 days following Dose 1, at the next contact or by mail.
- Recording of any prior or concomitant medication or vaccination administered in the CRF.
- Reporting of SAEs.

Day 30 (Return of diary cards/Phone Contact)

- Recording of all AEs occurring from Day 0 – Day 30 after Dose 1.
- Parents/guardians will be contacted by phone if the investigator does not receive the diary cards.
- The investigator will verify the diary card and transcribe the information into the appropriate sections of the CRF, in English.
- Recording of concomitant medication/vaccination administered in the CRF.

- Recording of SAEs.
- PMS conclusion for infants who have received one dose of the vaccine prior to the start of the PMS and have received the second dose of the vaccine at Visit 1 or if the investigator confirms that the infant will not be administered the second dose at the same centre.

Visit 2: *Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe)* vaccination **(Amendment 4: 23 February 2012)**

- Checking of contraindications to vaccination.
- Recording of body temperature (measured by oral/axillary/tympanic route).
- Vaccination:
  - One dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be administered orally according to instructions specified in section 6.2.
  - Infants will be allowed to receive concomitant vaccinations.

  The vaccinees will be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.
- Diary cards will be provided to the parents/guardians of all subjects to record information on AEs occurring on the day of Dose 2 and the following 30 days.
- The infants' parents/guardians will be instructed to contact the investigator immediately should the infant manifest any signs or symptoms they perceive as serious. The parents/guardians should be instructed to return the completed diary card to the investigator 30 days following Dose 2, at the next contact or by mail.
- Recording of any concomitant medication or vaccination administered in the CRF.
- Reporting of SAEs.

Day 30 after Visit 2 (Return of diary cards/Phone Contact)

- Recording of all AEs occurring from Day 0 – Day 30 after Dose 2.
- Parents/guardians will be contacted by phone if the investigator does not receive the diary cards.
- The investigator will verify the diary card and transcribe the information into the appropriate sections of the CRF, in English.
- Recording of concomitant medication/vaccination administered in the CRF.
- Recording of SAEs.
- PMS conclusion.

5.6. Sample handling and analysis

Not applicable.

6. INDICATION AND DOSAGE/ADMINISTRATION

6.1. Rotarix

Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** to be used in this PMS has been developed and manufactured by GSK Biologicals. **(Amendment 4: 23 February 2012)**

The Quality Control Standards and Requirements for the vaccine are described in separate release protocols and the required approvals have been obtained.

Commercial vaccines are assumed to comply with the specifications given in the manufacturer's Summary of Product Characteristics.

Table 2 presents the detailed formulation of the HRV vaccine.

Table 2 Composition of GSK Biologicals' HRV vaccine

Composition	Compound Objective	Ingredient	Reference	Quantity
Glass container	Active substance	Live attenuated human rotavirus (RIX4414 strain)	GSK Monograph	not less than $10^{6.0}$ $CCID_{50}$

$CCID_{50}$: median Cell Culture Infective Dose (quantity of virus causing infection in 50% of exposed cells)

6.2. Dosage and administration

Rotarix™ ***or Rotarix™ liquid formulation (oral suspension) or Rotarix™ liquid formulation (prefilled syringe)*** will be administered twice orally as per the prescribing information in Korea.

- First vaccination will be given to infants aged 6 weeks and above.
- Second vaccination will be given at least 4 weeks after Dose 1. Administration of Dose 2 is preferably given before the age of 16 weeks.

  Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** should be given before 24 weeks of age.

The vaccinees will be observed closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Refer to the prescribing information for details on the dosage and administration of the vaccine. **(Amendment 4: 23 February 2012)**

6.3. Storage

The vaccine must be stored in an airtight container at the defined temperature range (i.e. +2 to +8°C). It should be protected from light.

6.4. Subject number allocation

Target enrolment will be **at least** 3000 evaluable infants. All infants enrolled into the PMS will receive Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccine in routine clinical practice settings. **(Amendment 4: 23 February 2012)**

Subject numbers will be allotted in a sequential manner.

6.5. Method of blinding and breaking the blind

Not applicable.

6.6. Replacement of unusable vaccine doses

Not applicable. The vaccine will be purchased by the infant's parent/guardian.

6.7. Packaging

Not applicable.

6.8. Vaccine accountability

Not applicable.

6.9. Concomitant medication/treatment

At each visit/contact, the investigator should question the infant's parents/guardian about any medication(s) taken.

All concomitant medication, with the exception of vitamins and/or dietary supplements, administered at ANY time during the period starting with administration of each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** after enrolling into the PMS up to the end of the follow-up period for AEs are to be recorded with generic name of the medication (trade names are allowed for combination drugs, i.e. multi-component drugs), medical indication, total daily dose, route of administration, start and end dates of treatment. **(Amendment 4: 23 February 2012)**

Any vaccine administered in the period beginning 30 days preceding each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** and ending one month (minimum 30 days) after is to be recorded with trade name, route of administration and date(s) of administration. **(Amendment 4: 23 February 2012)**

A prophylactic medication is a medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination (e.g. an anti-pyretic is considered to be prophylactic when it is given in the absence of fever [Oral temperature <37.5°C/Axillary temperature <37.5°C/Tympanic temperature on oral setting <37.5°C] and any other symptom, to prevent fever from occurring). Any concomitant medication administered prophylactically in anticipation of reaction to the vaccination must be recorded in the CRF with generic name of the medication (trade names are allowed for combination drugs only), total daily dose, route of administration, start and end dates of treatment and coded as 'Prophylactic'.

During the period starting with administration of each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** up to the end of the follow-up period for AEs, concomitant medication administered for the treatment of an AE must be recorded in the CRF with generic name of the medication (trade names are allowed for combination drugs only), medical indication (including which AE), total daily dose, route of administration, start and end dates of treatment. Similarly, concomitant medication administered for the treatment of an SAE, at any time, must be recorded on the SAE Report Form. Refer to Section 8.2 for definition of SAE. **(Amendment 4: 23 February 2012)**

7. HEALTH ECONOMICS

Not applicable.

8. ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

The investigator is responsible for the detection and documentation of events meeting the criteria and definition of an AE or SAE as provided in this protocol. During the PMS, when there is a safety evaluation, the investigator or site staff will be responsible for detecting AEs and SAEs, as detailed in this section of the protocol.

Each infant's parents/guardians will be instructed to contact the investigator immediately should the infant manifest any signs or symptoms they perceive as serious.

8.1. Definition of an adverse event

An AE is any untoward medical occurrence, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.

Examples of an AE include:

- Significant or unexpected worsening or exacerbation of the condition/indication under the PMS.
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after medicinal product administration even though it may have been present prior to the start of the PMS.
- Signs, symptoms, or the clinical sequelae of a suspected interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either medicinal product or a concurrent medication (overdose per se should not be reported as an AE/SAE).
- Significant failure of expected pharmacological or biological action.
- Signs, symptoms temporally associated with vaccine administration.

Examples of an AE DO NOT include:

- Medical or surgical procedure (e.g. endoscopy, appendectomy); the condition that leads to the procedure is an AE.
- Situations where an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the PMS that do not worsen.

Example of events to be recorded in the medical history section of the CRF:

- Pre-existing conditions or signs and/or symptoms present in a subject prior to the start of the PMS (i.e. prior to the first vaccination).

8.2. Definition of a serious adverse event

An SAE is any untoward medical occurrence that:

a. results in death,

b. i**s** life-threatening,

NOTE: *The term 'life-threatening' in the definition of 'serious' refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.*

c. requires hospitalisation or prolongation of existing hospitalisation,

NOTE: In general, hospitalisation signifies that the subject has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or out-patient setting. Complications that occur during hospitalisation are AEs. If a complication prolongs hospitalisation or fulfils any other serious criteria, the event is

serious. When in doubt as to whether "hospitalisation" occurred or was necessary, the AE should be considered serious.

Hospitalisation for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.

d. results in disability/incapacity, or

NOTE: The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhoea, influenza, and accidental trauma (e.g. sprained ankle) which may interfere or prevent everyday life functions but do not constitute a substantial disruption.

(Amendment 4: 23 February 2012)

Medical or scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardize the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation.

8.2.1. Disease-related events or outcomes not qualifying as serious adverse events

Not applicable.

8.3. Lack of efficacy

"Lack of efficacy" per se will not be reported as an AE. The signs and symptoms or clinical sequelae resulting from lack of efficacy will be reported if they fulfil the AE or SAE definition (including clarifications).

8.4. Clinical laboratory parameters and other abnormal assessments qualifying as adverse events and serious adverse events

Abnormal laboratory findings (e.g. clinical chemistry, haematology, urinalysis) or other abnormal assessments (e.g. ECGs, X-rays, vital signs etc) that are judged by the investigator to be clinically significant will be recorded as AEs or SAEs if they meet the definition of an AE, as defined in Section 8.1 or SAE, as defined in Section 8.2. Clinically significant abnormal laboratory findings or other abnormal assessments that are detected during the PMS or are present at baseline and significantly worsen following the start of the PMS will be reported as AEs or SAEs.

The investigator should liaise with treating physician (if different from investigator) in all cases where PMS participants are hospitalised with SAE.

The investigator will exercise his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment is clinically significant.

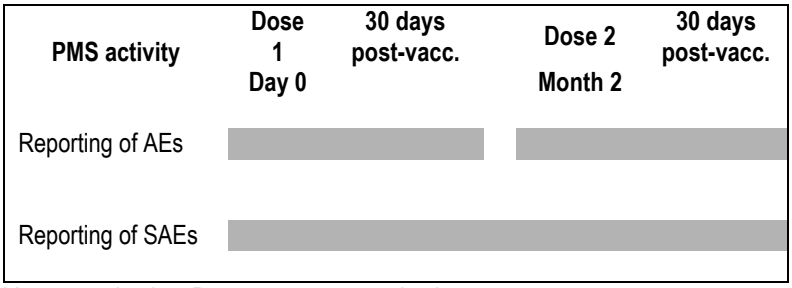
8.5. Time period, frequency, and method of detecting adverse events and serious adverse events

All AEs occurring within 31 days (Day 0 – Day 30) following administration of each dose of vaccine received after enrolling into the PMS must be recorded into the Adverse Event form in the infant's CRF, irrespective of intensity or whether or not they are considered vaccination-related.

The standard time period for collecting and recording SAEs will begin at the first receipt of ***Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** and will end at the last contact for each infant. See Section 8.8 for instructions for reporting and recording SAEs. **(Amendment 4: 23 February 2012)**

An overview of the protocol-required reporting periods for adverse events and serious adverse events is given in Table 3.

Table 3 Reporting periods for adverse events and serious adverse events



Vacc.: vaccination; Post-vacc.: post-vaccination

The investigator will inquire about the occurrence of AEs/SAEs at every visit/contact during the PMS.

All AEs either observed by the investigator or one of his clinical collaborators or reported by the infant's parent/guardian spontaneously or in response to a direct question will be evaluated by the investigator. AEs not previously documented in the PMS will be recorded in the Adverse Event form within the infant's CRF. The nature of each event, date and time (where appropriate) of onset, outcome, intensity and relationship to vaccination should be established. Details of any corrective treatment should be recorded on the appropriate page of the CRF. Refer to Section 6.9.

As a consistent method of soliciting AEs, the infant's parent/guardian should be asked a non-leading question such as:

"Has your child acted differently or felt different in any way since receiving the vaccine or since the last visit?"

N.B. The investigator should record only those AEs having occurred within the time frame defined above.

AEs already documented in the CRF, i.e. at a previous assessment, and designated as "not recovered/not resolved" or "recovering/resolving" should be reviewed at subsequent visits, as necessary. If these have resolved, the documentation in the CRF should be completed.

When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation (e.g. hospital progress notes, laboratory, and diagnostics reports) relative to the event. The investigator will then record all relevant information regarding an AE/SAE on the CRF or SAE Report Form as applicable. It is not acceptable for the investigator to send photocopies of the infant's medical records to GSK Biologicals in lieu of the appropriate completed AE/SAE pages. However, there may be instances when copies of medical records for certain cases are requested by GSK Biologicals. In this instance, all subject identifiers will be blinded on the copies of the medical records prior to submission to GSK Biologicals.

The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis should be documented as the AE/SAE and not the individual signs/symptoms.

8.6. Evaluating adverse events and serious adverse events

8.6.1. Assessment of intensity

The investigator will make an assessment of the maximum intensity that occurred over the duration of the event for all AEs, i.e. (i.e. non-serious adverse events) reported during the PMS. The assessment will be based on the investigator's clinical judgement.

The intensity of each AE recorded in the CRF, as applicable, should be assigned to one of the following categories:

1 (mild)	=	An AE which is easily tolerated by the infant, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE which is sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE which prevents normal, everyday activities. (In a young child, such an AE would, for example, prevent attendance at school/kindergarten/a day-care centre and would cause the parents/guardians to seek medical advice).

An AE that is assessed as Grade "3" (severe) should not be confused with a SAE. Grade "3" is a category utilised for rating the intensity of an event. An event is defined as 'serious' when it meets one of the pre-defined outcomes as described in Section 8.2.

8.6.2. Assessment of causality

The investigator is obligated to assess the relationship between Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** and the occurrence of each AE/SAE. The investigator will use clinical judgement to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors and the temporal relationship of the event to Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be considered and investigated. The investigator will also consult the Product Information, for marketed products, in the determination of his/her assessment. **(Amendment 4: 23 February 2012)**

There may be situations when a SAE has occurred and the investigator has minimal information to include in the initial report to GSK Biologicals. However, it is very important that the investigator always makes an assessment of causality for every event prior to submission of the SAE to GSK Biologicals. The investigator may change his/her opinion of causality in light of follow-up information, amending the SAE information accordingly. The causality assessment is one of the criteria used when determining regulatory reporting requirements.

In case of concomitant administration of multiple vaccines, it may not be possible to determine the causal relationship of general AEs to the individual vaccines administered. The investigator should, therefore, assess whether the AE could be causally related to vaccination rather than to the individual vaccines.

Causality of all AEs should be assessed by the investigator using the following question:

Is there a reasonable possibility that the AE may have been caused by Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***?

Assessment of causality of these AEs will be done to reflect the requirement of KFDA to assess the relationship of the AEs. **(Amendment 4: 23 February 2012)**

NOTE: The use of the term "drug" here refers to the vaccine.

As per KFDA requirements, causality will be assessed as:

Certain:

- The relationship of the administration and use of the drug is reasonable and it is not able to be explained by other medication, chemical substances or concomitant disease, it shows clinically reasonable response on withdrawal of the drug, the decisive case in the Pharmacological or phenomenological aspect on re-challenge of the drugs if needed.

Probable/Likely:

- The temporal sequence of the administration and use of the drug is appropriate and it does not seem that it is accompanied by other medications, chemical substances or concomitant disease, in the case that shows clinically appropriate response on withdrawal of the drug (no information for re-challenge).

Possible:

- The temporal sequence of the administration and use of the drug is appropriate but it is also able to be explained by other medications, chemical substances or concomitant disease, and information related to withdrawal of the drug is insufficient or vague.

Unlikely:

- It is a transitory case which may not have causality with the administration and use of the drug, it is also able to be explained reasonably by other medications, chemical substances or latent disease.

Conditional/Unclassified:

- In the case that more information is needed for a proper evaluation or additional information is under review.

Unassessible/Unclassifiable:

- In the case that could not be judged due to insufficient or conflicting information and no way to complement or validate.

8.6.3. Medically attended visits

For each AE the infant experiences, the infant's parents/guardians will be asked if they received medical attention defined as hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information will be recorded in the CRF.

8.7. Follow-up of adverse events and serious adverse events and assessment of outcome

After the initial AE/SAE report, the investigator is required to proactively follow each infant and provide further information to GSK Biologicals on the infant's condition.

All AEs and SAEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving will be reviewed at subsequent visits/contacts.

Investigators will follow-up infants:

- with SAEs or infants withdrawn from the PMS as a result of an AE, until the event has resolved, subsided, stabilised, disappeared, the event is otherwise explained, or the infant is lost to follow-up;
- or, in the case of other non-serious AEs, until they complete the PMS or they are lost to follow-up.

Clinically significant laboratory abnormalities will be followed up until they have returned to normal, or a satisfactory explanation has been provided. Additional information (including but not limited to laboratory results) relative to the subsequent course of such an abnormality noted for any infant must be made available to the Study Monitor.

GSK Biologicals may request that the investigator perform or arrange for the conduct of supplemental measurements and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE or SAE. The investigator is obliged to assist. If an infant dies during participation in the PMS or during a recognised follow-up period, GSK Biologicals will be provided with a copy of any available post-mortem findings, including histopathology.

New or updated information will be recorded on the originally completed SAE Report Form. All changes on the SAE Report Form should be signed and dated by the investigator. The updated SAE Report Form should be resent to GSK Biologicals within 24 hours of receipt of the follow-up information as outlined in Section 8.8.1.

Outcome of any non-serious AE occurring within 31 days (Day 0 – Day 30) days post-vaccination or any SAE reported during the entire PMS will be assessed as:

- Recovered/resolved
- Not recovered/not resolved
- Recovering/resolving
- Recovered with sequelae/resolved with sequelae
- Fatal (SAEs only)
- Unknown

8.8. Prompt reporting of serious adverse events to GSK Biologicals

8.8.1. Time frames for submitting serious adverse event reports to GSK Biologicals

SAEs will be reported promptly to GSK once the investigator determines that the event meets the protocol definition of an SAE. The investigator or designate will fax the SAE reports to GSK Biologicals' Study Contact for Serious Adverse Event Reporting WITHIN 24 HOURS OF HIS/HER BECOMING AWARE OF THESE EVENTS. Additional or follow-up information relating to the initial SAE report is also to be reported to the GSK Biologicals' Study Contact for Serious Adverse Event Reporting within 24 hours of receipt of such information.

8.8.2. Completion and transmission of serious adverse event reports to GSK Biologicals

Once an investigator becomes aware that a SAE has occurred in an infant, she/he will report the information to GSK within 24 hours as outlined in Section 8.8.1. The SAE Report Form will always be completed as thoroughly as possible with all available details of the event, signed by the investigator (or designee), and forwarded to GSK within the designated time frames. If the investigator does not have all information regarding an SAE, he/she will not wait to receive additional information before notifying GSK of the event and completing the form. The form will be updated when additional information is received and forwarded to GSK WITHIN 24 HOURS as outlined in Section 8.8.1.

The investigator will always provide an assessment of causality at the time of the initial report as described in Section 8.6.2.

Facsimile (Fax) transmission of the SAE Report Form is the preferred method to transmit this information to the Study Contact for Reporting SAEs. In rare circumstances and in the absence of facsimile equipment, notification by telephone is acceptable, with a copy of the SAE Report Form sent by overnight mail. Initial notification via the telephone does not replace the need for the investigator to complete and sign the SAE Report Form within 24 hours as outlined in Section 8.8.1.

In the event of a death determined by the investigator to be related to vaccination, sending of the fax must be accompanied by telephone call to the Study Contact for Reporting SAEs.

Study Contact for Reporting SAEs
Refer to the Sponsor Information Sheet
Back-up Study Contact for Reporting SAEs
GSK Biologicals Clinical Safety and Pharmacovigilance Fax: PPD or PPD **24/24 hour and 7/7 day availability**

8.9. Regulatory reporting requirements for serious adverse events

The investigator will promptly report all SAEs to GSK in accordance with the procedures detailed in Section 8.8. GSK Biologicals has a legal responsibility to promptly notify, as appropriate, both the local regulatory authority and other regulatory agencies about the safety of a product under clinical investigation. Prompt notification of SAEs by the investigator to the Study Contact for Reporting SAEs is essential so that legal obligations and ethical responsibilities towards the safety of other subjects are met.

The investigator, or responsible person according to local requirements, will comply with the applicable local regulatory requirements related to the reporting of SAEs to the IRB/IEC and, if required, to the applicable government authority.

8.10. Post-PMS adverse events and serious adverse events

A post-PMS AE/SAE is defined as any event that occurs outside of the AE/SAE detection period defined in Section 8.5. Investigators are not obligated to actively seek AEs or SAEs in former PMS participants.

However, if the investigator learns of any SAE, including a death, at any time after an infant has been discharged from the PMS, and he/she considers the event reasonably related to Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***, the investigator will promptly notify the Study Contact for Reporting SAEs. **(Amendment 4: 23 February 2012)**

8.11. Pregnancy

Not applicable.

8.12. Treatment of adverse events

Treatment of any adverse event is at the sole discretion of the investigator and according to current good medical practice. Any medication administered for the treatment of an AE should be recorded in the infant's CRF. Refer to Section 6.9.

9. SUBJECT COMPLETION AND WITHDRAWAL

9.1. Subject completion

An infant who has the 30 day safety contact after the second Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination is considered to have completed the PMS. **(Amendment 4: 23 February 2012)**

9.2. Subject withdrawal

9.2.1. Subject withdrawal from the PMS

A subject qualifies as a 'withdrawal' from the PMS if the second Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination is not given in this PMS or when the 30 day safety contact after the last Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** dose does not take place. **(Amendment 4: 23 February 2012)**

Investigators will make an attempt to contact those subjects who do not return for scheduled visits.

Information relative to the withdrawal will be documented on the PMS Conclusion page of the CRF. The investigator will document whether the decision to withdraw from the PMS was made by the infant's parent or guardian or the investigator and which of the following possible reasons was responsible for withdrawal:

- serious adverse event
- non-serious adverse event
- consent withdrawal, not due to an adverse event
- moved from the PMS area
- lost to follow-up
- other (specify).

9.2.2. Subject withdrawal from Rotarix

A 'withdrawal' from Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** is any infant who does not receive the second Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** dose in the PMS. An infant withdrawn from Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled***

syringe) may not necessarily be withdrawn from the PMS as further procedures or follow-up may be performed (safety) if planned in the protocol.

Information relative to premature discontinuation of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be documented on the Vaccine Administration page of the CRF. The investigator will document whether the decision to discontinue further vaccination was made by the infant's parent or guardian or the investigator and which of the following possible reasons was responsible for withdrawal: **(Amendment 4: 23 February 2012)**

- serious adverse event,
- non-serious adverse event,
- other (specify).

10. DATA EVALUATION: CRITERIA FOR EVALUATION OF OBJECTIVES

10.1. Endpoints

- Occurrence of AEs during the 31-day (Day 0 – Day 30) follow-up period after each vaccine dose according to Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of SAEs during the entire PMS period.

10.2. Estimated sample size

According to KFDA regulation requirement, at least 3000 evaluable subjects will be recruited for the PMS.

Table 4 presents the exact two-sided 95% confidence interval for a sample size of 3000 subjects. **(Amendment 4: 23 February 2012)**

Table 4 Exact two-sided 95% CI for a sample size of 3000 subjects

Observed rate expressed as a percentage (number of subjects reporting at least one symptom)	Exact two-sided 95% CI for this observed rate for a sample size of 3000 subjects	
	Lower limit (LL)	Upper limit (UL)
50(1500)	48.2	51.8
55(1650)	53.2	56.8
60(1800)	58.2	61.8
65(1950)	63.3	66.7
70(2100)	68.3	71.6
75(2250)	73.4	76.5
80 (2400)	78.5	81.4
85(2550)	83.7	86.3

10.3. Cohorts to be evaluated

10.3.1. Total Vaccinated cohort

The total vaccinated cohort will include all vaccinated subjects with at least one dose of ***Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** administration documented: **(Amendment 4: 23 February 2012)**

- a safety analysis based on the total vaccinated cohort will include all vaccinated subjects.

10.4. Derived and transformed data

Infants who missed reporting symptoms (AEs or concomitant medications) will be treated as infants without symptoms (AEs or concomitant medications, respectively). In case of significant non-compliance of PMS procedures for reporting symptoms, the analysis plan will be reassessed to ensure more accurate reporting of PMS data by further analysis.

10.5. Final analyses

Statistical analyses will be performed as per the GSK standards as well as to reflect the requirements of KFDA.

10.5.1. Analysis of demographics/baseline characteristics

The mean, range and standard deviation of age in weeks at each dose will be calculated. The racial, rotavirus vaccination history and gender composition of the vaccinated subjects will be also presented.

The distribution of subjects enrolled among the PMS centres will be tabulated.

10.5.2. Analysis of safety

For all infants enrolled prior to Amendment 3 dated 10 February 2010, the following statistical analysis will be performed:

The overall incidence, with exact 95% confidence interval (CI), of any adverse events (solicited or unsolicited) during the 8-day solicited follow-up period will be tabulated, for each dose, for overall doses and per subject. The same calculations will be done for any adverse events (solicited or unsolicited); rated as grade “3” and for those assessed as causally related to vaccination.

The incidence, with exact 95% CI, of each individual solicited general symptom, will be calculated, over the solicited follow-up period, after each dose, for all doses and per subject. The same calculations will be done for each individual solicited general symptom rated as grade “3” and for each individual solicited general symptom related to vaccination.

The verbatim reports of unsolicited symptoms will be reviewed by a physician and the signs and symptoms will be coded according to MedDRA. Every verbatim term will be matched with the appropriate Preferred Term. The percentage of subjects with unsolicited symptoms occurring within 31 days with its exact 95% CI will be tabulated by preferred term. Similar tabulation will be done for unsolicited symptoms with relationship to vaccination and for unsolicited adverse events rated as grade 3.

The percentage of subjects who received at least one concomitant medication/vaccination during the 8-day (Day 0 – Day 7) solicited follow-up period will be tabulated by type of medication, with exact 95% CI. Similar tabulations will be done for subjects who receive concomitant medication/vaccination during the entire PMS period.

Serious adverse events and withdrawals due to adverse events reported during the PMS period will be described in detail.

For all subjects enrolled after the Amendment 3 dated 10 February 2010, the following statistical analysis will be performed:

The AEs/SAEs collected will be analysed in the study report according to the expectedness and unexpectedness criteria. Refer to the Glossary of Terms for the definitions of expected AEs and unexpected AEs.

The overall incidence, with exact 95% confidence interval (CI), of any adverse events occurring within 31 days will be tabulated, for each dose, for overall doses and per subject. The same calculations will be done for any adverse events; rated as grade “3” and for all the causality grading mandated by KFDA.

The verbatim reports of AEs will be reviewed by a physician and the signs and symptoms will be coded according to MedDRA. Every verbatim term will be matched with the appropriate Preferred Term. The percentage of subjects with AEs occurring within 31 days with its exact 95% CI will be tabulated by preferred term. Similar tabulation will be done for AEs rated as grade 3 and for all causality grading mandated by KFDA.

The percentage of subjects who received at least one concomitant medication/vaccination during the 30 day follow-up period will be tabulated by type of medication, with exact 95% CI. Similar tabulations will be done for subjects who receive concomitant medication/vaccination during the entire PMS period.

Serious adverse events and withdrawals due to adverse events reported during the PMS period will be described in detail.

In addition, specific statistical analyses (e.g. AEs classified by gender, past medical history, concomitant medication/vaccination etc) will be performed to reflect the KFDA requirements.

10.6. Planned interim analysis

Annual reports will be written for 6 years. The last annual report will be replaced by a comprehensive report. All analyses described above will be performed on cleaned data

for each annual report. The analysis, including individual data listings, will be cumulative and based on the cohort for vaccinated subjects for which the PMS conclusion page has been received at GSK before the pre-defined cut-off date. All reports will be sent to the GSK Biologicals' Central Safety and Pharmacovigilance (BCSP).

11. ADMINISTRATIVE MATTERS

To comply with local rules, regulations, relevant GSK SOPs/Policies/Guidance, important administrative obligations relating to investigator responsibilities, monitoring, archiving data, audits, confidentiality and publications must be fulfilled. See Appendix B for details.

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Appendix A Administrative Matters

I. Responsibilities of the Investigator

- To ensure that he/she has sufficient time to conduct and complete the PMS and has adequate staff and appropriate facilities and equipment which are available for the duration of the PMS and to ensure that other studies do not divert essential subjects or facilities away from the PMS at hand.
- To prepare and maintain adequate subject source data or raw data designed to record observations, and other data pertinent to the PMS.
- To co-operate with a representative of GSK Biologicals in the monitoring process of the PMS and in resolution of queries about the data.
- To conduct the study in compliance with the protocol any amendment**,** all applicable regulatory requirements and GSK SOPs/Policies and Guidance.
- To permit drug regulatory agencies and GSK audits.

II. Protocol Amendments and Administrative changes

- No changes to the protocol will be allowed unless discussed in detail with the GSK Biologicals' Clinical Development Manager/Medical Monitor and filed as an amendment/administrative change to this protocol.
- Any amendment/administrative change to the protocol will be adhered to by the participating centre(s) and will apply to all subjects. Written IRB approval of protocol amendments is required prior to implementation, except where the sites do not have IRB.

III. Sponsor's Termination of PMS

GSK Biologicals reserves the right to temporarily suspend or prematurely discontinue this PMS either at a single site or at all sites at any time for reasons including, but not limited to, safety or ethical issues or severe non-compliance. Reasons for suspension or early termination will be documented in the PMS file at GSK Biologicals.

If GSK Biologicals determines that suspension or early termination is needed, GSK Biologicals will discuss this with the Investigator (including the reasons for taking such action). When feasible, GSK Biologicals will provide advance notification to the investigator of the impending action prior to it taking effect.

GSK Biologicals will promptly inform, via written communication, all investigators and/or institutions conducting the PMS, if the PMS is suspended or terminated for safety reasons, and will also inform the regulatory authorities of the suspension or termination of the PMS and the reason(s) for the action. If required by applicable regulations, the investigator must inform the IRB promptly (except where the sites do not have IRB) and provide the reason for the suspension or termination.

If the study is prematurely discontinued, all PMS data must be returned to GSK. Financial compensation to investigators and/or institutions will be in accordance with the agreement established between the investigator and/or institutions and GSK.

IV. Case Report Form Instructions

Prior to screening the first potential participant, the investigator will provide the Site Monitor with a list (Site Staff Signature Sheet) showing the name and title, signature and initials of all site staff who have a critical effect on the conduct of the PMS and to whom the investigator has delegated significant PMS related duties such as entering data on the CRFs or changing entries on CRFs. If the authorised individuals should change during the PMS, the investigator is to inform GSK Biologicals GSK Biologicals' representative of the specific change(s).

CRFs (and subject diary cards, if applicable), will be supplied by GSK Biologicals for recording all data. It is the responsibility of the investigator or co-investigator to ensure that data are legible, accurate, adequately recorded and, when entered on paper copy, completely filled in with a black ink fountain or ballpoint pen.

Errors must be corrected by drawing a single line through the incorrect entry and writing in the new value/data positioned as close to the original as possible. The correction must then be initialled and dated (and justified, whenever possible), where necessary, by the authorised individual making the change. The original entry must not be obliterated, overwritten or erased when a correction is made.

When a subject completes a visit, it is anticipated that relevant sections of the CRF will be completed by the investigator (or designated staff as documented in the Site Staff Signature Sheet) as soon as possible after the last data becoming available. Similarly, when a subject completes a PMS, it is anticipated that all relevant CRF pages will be completed promptly after the last data becoming available.

As soon as the subject has completed/withdrawn from the PMS and the CRF is completed, the investigator or medically qualified sub-investigator to whom this task has been delegated will sign the PMS conclusion pages of the CRF to confirm that they have reviewed the data and that the data are complete and accurate. In all cases the investigator remains accountable for the PMS data collected.

An original (top copy) CRF or log sheets must be submitted for all subjects who have undergone protocol specific procedures, whether or not the subject completed the PMS.

While completed CRFs are reviewed by a GSK Biologicals' professional monitor at the site, errors detected by subsequent in-house CRF review may necessitate clarification or correction of errors with documentation and approval by the investigator or appropriately qualified designee as documented on the Site Staff Signature Sheet. In all cases, the investigator remains accountable for the PMS data. Wherever possible the investigator should assist in the clarification or correction of errors detected after PMS finalisation promptly after being brought to the attention of the investigator.

Any questions or comments related to the CRF should be directed to the assigned Site Monitor.

V. Monitoring by GSK Biologicals

To ensure compliance with the protocol, monitoring visits by a professional representative of the sponsor will be scheduled to take place early in the PMS, during the PMS at appropriate intervals and after the last subject has completed the PMS. It is anticipated that monitoring visits will occur at a frequency defined and communicated to the investigator before PMS start.

These visits are for the purpose of confirming that GSK Biologicals' sponsored studies are being conducted in accordance with the ethical principles, the applicable regulatory requirement(s) and relevant GSK SOPs/Policies and Guidance (verifying continuing compliance with the protocol, amendment(s), verifying that the site staff and facilities continue to be adequate to conduct the PMS. Direct access to all PMS-related site and source data/documents is mandatory for the purpose of monitoring review. The monitor will perform a CRF review and a Source Document verification (verifying CRF entries by comparing them with the source data/documents that will be made available by the investigator for this purpose: any data item for which the CRF will serve as the source must be identified, agreed and documented. Data to be recorded directly onto the CRF pages will be specified in writing preferably in the source documentation agreement form that is contained in both the monitor's and investigator's file. The investigator must ensure provision of reasonable time, space and adequate qualified personnel for monitoring visits. Source data verification (SDV) must be conducted using a GSK standard SDV sampling strategy (as defined at the study start in the study specific monitoring guidelines) in which monitors will perform partial SDV for all subjects and full SDV for selected subjects.

VI. Archiving of Data

Following closure of the PMS, the investigator must maintain all site records in a safe and secure location. The records must be maintained to allow easy and timely retrieval, when needed (e.g., audit or inspection), and, whenever feasible, to allow any subsequent review of data in conjunction with assessment of the facility, supporting systems, and staff. Where permitted by applicable laws/regulations or institutional policy, some or all of these records can be maintained in a validated format other than hard copy (e.g. microfiche, scanned, for example); however, caution needs to be exercised before such action is taken. The investigator must assure that all reproductions are legible and are a true and accurate copy of the original, and meet accessibility and retrieval standards, including re-generating a hard copy, if required. Furthermore, the investigator must ensure there is an acceptable back-up of these reproductions and that an acceptable quality control process exists for making these reproductions.

GSK will inform the investigator/ institution of the time period for retaining these records to comply with all applicable regulatory requirements. However, the investigator/ institution should seek the written approval of the sponsor before proceeding with the disposal of these records. The minimum retention time will meet the strictest standard applicable to that site for the study, as dictated by ICH GCP E6 Section 4.9, any

institutional requirements or applicable laws or regulations, or GSK standards/procedures; otherwise, the minimum retention period will default to 3 years.

The investigator/ institution must notify GSK of any changes in the archival arrangements, including, but not limited to, the following: archival at an off-site facility, transfer of ownership of the records in the event the investigator leaves the site.

VII. Audits

For the purpose of compliance with Regulatory Agency Guidelines and relevant GSK SOPs/Policies and Guidance it may be necessary for GSK or a Drug Regulatory Agency to conduct a site audit. This may occur at any time from start to after conclusion of the PMS.

When an investigator signs the protocol, he agrees to permit drug regulatory agencies and GSK audits, providing direct access to source data/ documents. Furthermore, if an investigator refuses an inspection, his data will not be accepted in support of a New Drug Registration and/or Application, Biologics Licensing Application.

Having the highest quality data and studies are essential aspects of vaccine development. GSK has a Regulatory Compliance staff who audit investigational sites. Regulatory Compliance assesses the quality of data with regard to accuracy, adequacy and consistency. In addition, Regulatory Compliance assures that GSK Biologicals' sponsored studies are in accordance with relevant regulatory/guidelines and relevant GSK SOPs/Policies and Guidance are being followed.

GSK Biologicals will gladly help investigators prepare for an inspection.

VIII. Ownership, Confidentiality and Publication

Ownership:
All information provided by GSK and all data and information generated by the site as part of the PMS (other than a subject's medical records) are the sole property of GSK.

All rights, title, and interests in any inventions, know-how or other intellectual or industrial property rights which are conceived or reduced to practice by site staff during the course of or as a result of the PMS are the sole property of GSK, and are hereby assigned to GSK.

If a written contract for the conduct of the PMS which includes ownership provisions inconsistent with this statement is executed between GSK and the site, that contract's ownership provisions shall apply rather than this statement.

Confidentiality:
Documented evidence that a potential investigator is aware and agrees to the confidential nature of the information related to the PMS must be obtained by means of a confidentiality agreement.

All information provided by GSK and all data and information generated by the site as part of the PMS (other than a subject's medical records) will be kept confidential by the investigator and other site staff. This information and data will not be used by the investigator or other site personnel for any purpose other than conducting the PMS. These restrictions do not apply to: (1) information which becomes publicly available through no fault of the investigator or site staff; (2) information which it is necessary to disclose in confidence to an IRB solely for the evaluation of the PMS; (3) information which it is necessary to disclose in order to provide appropriate medical care to a subject; or (4) PMS results which may be published as described in the next paragraph. If a written contract for the conduct of the PMS which includes confidentiality provisions inconsistent with this statement is executed, that contract's confidentiality provisions shall apply rather than this statement.

Publication:
For multicentre studies, the first publication or disclosure of results shall be a complete, joint multicentre publication or disclosure coordinated by GSK. Thereafter, any secondary publications will reference the original publication(s).

Prior to submitting for publication, presentation, use for instructional purposes, or otherwise disclosing the results generated by the site (collectively, a "Publication"), the investigator shall provide GSK with a copy of the proposed Publication and allow GSK a period to review the proposed Publication (at least 21 (twenty-one) days [or at least 15 (fifteen) working days for abstracts/posters/presentations]. Proposed Publications shall not include either GSK confidential information other than the results or personal data on any subject, such as name or initials.

At GSK's request, the submission or other disclosure of a proposed Publication will be delayed a sufficient time to allow GSK to seek patent or similar protection of any inventions, know-how or other intellectual or industrial property rights disclosed in the proposed Publication.

If a written contract for the conduct of the PMS, which includes publication provisions inconsistent with this statement is executed, that contract's publication provisions shall apply rather than this statement.

Appendix B Overview of the Recruitment Plan

- The PMS will be conducted at multiple centres in Korea.
- Infants aged 6 weeks or above at the time of first vaccination will be enrolled in this PMS.
- Infants recruited by investigators will be given the vaccination as a part of their normal practice.
- Target enrolment will be at least 3000 evaluable infants.
- The PMS is required to be conducted in at least one hospital (with IRB oversight) in order for PMS to be conducted in private clinics (with no IRB).
- The recruitment will be monitored by the study monitor.

Appendix C Prescribing Information

Refer to locally approved prescribing information.

Appendix D Amendments and Administrative Changes to the Protocol

GlaxoSmithKline Biologicals Clinical Research & Development **Protocol Amendment**	
eTrack number and abbreviated title	111700 (Rota-070 PMS)
Title	Reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.
Detailed Title:	Open, multi-centric, post-marketing surveillance (PMS) to monitor the reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.
Amendment number:	Amendment 1
Amendment date:	09 May 2008
Co-ordinating author:	PPD Scientific Writer
Rationale/background for changes: The protocol was amended to comply with the Korean Food and Drug Administration (KFDA) requirements.	
Amended text has been included in *bold italics* in the following section(s): Section 8.6.2 Assessment of causality	

Section 8.6.2 Assessment of causality

1. Definitely related:
   - There is evidence of exposure ~~to the vaccine~~ ***of the drug***.
   - The temporal sequence of the AE onset relative to administration of the ~~vaccine~~ ***drug*** is reasonable
   - AE is more likely explained by the ~~vaccine~~ ***drug*** than by another cause
   - ***The AE is subsiding or disappearing on withdrawal of the drug***
   - Rechallenge (if feasible) is positive.
   - The AE shows a pattern consistent with previous knowledge of the ~~vaccine~~ ***drug*** or the ~~vaccine~~ ***drug*** class.

2. Probably related:
   - There is evidence of exposure ~~to the vaccine~~ ***of the drug***.
   - The temporal sequence of the AE onset relative to administration of the ~~vaccine~~ ***drug*** is reasonable
   - AE is more likely explained by the ~~vaccine~~ ***drug*** than by another cause
   - ***The AE is subsiding or disappearing on withdrawal of the drug***
3. Possibly related:
   - There is evidence of exposure ~~to the vaccine~~ ***of the drug***.
   - The temporal sequence of the AE onset relative to administration of the ~~vaccine~~ ***drug*** is reasonable
   - The AE could have been due to another equally likely cause
   - ***The AE is subsiding or disappearing on withdrawal of the drug (if performed)***
4. ~~Unlikely to be~~ ***Probably not*** related:
   - ***There is no evidence of exposure of the drug***
   - There is another more likely cause of the AE
   - ***The AE is not disappearing even on withdrawal of the drug (if performed) or ambiguous***
5. Unknown

GlaxoSmithKline Biologicals

Clinical Research & Development

Protocol Amendment

eTrack number and abbreviated title	111700 (Rota-070 PMS)
Title	Reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.
Detailed Title:	Open, multi-centric, post-marketing surveillance (PMS) to monitor the reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.
Amendment number:	Amendment 2
Amendment date:	13 October 2008
Co-ordinating author:	PPD Scientific Writer

Rationale/background for changes:

The protocol was amended to modify the timelines for the interim analysis thereby replacing bi-annual reports with annual reports. In addition, the protocol amendment investigator agreement page has been included in the protocol.

Section 10.6 Planned interim analysis

~~Bi-annual reports will be written for the first two years and~~ ***A***nnual reports will be written for ~~the remaining 4~~ ***6*** years. ~~A comprehensive report will be written at the end of 6 years.~~ ***The last annual report will be replaced by a comprehensive report.*** All analyses described above will be performed on cleaned data for each ~~bi-annual~~/annual report. The analysis, including individual data listings, will be cumulative and based on the cohort for vaccinated subjects for which the PMS conclusion page has been received at GSK before the pre-defined cut-off date. All reports will be sent to the GSK Biologicals' Central Safety and Pharmacovigilance (BCSP).

Protocol Amendment Investigator Agreement

I agree:

- ***To assume responsibility for the proper conduct of the study at this site.***
- ***To conduct the study in compliance with this protocol, any mutually agreed future protocol amendments, and with any other study conduct procedures provided by GlaxoSmithKline Biologicals (GSK Biologicals).***
- ***To ensure that all persons assisting me with the study are adequately informed about the GSK Biologicals' Rotarix™ and other study-related duties and functions as described in the protocol.***
- ***Not to implement any changes to the protocol without agreement from the sponsor and prior review and written approval from the Institutional Review Board (IRB) or Independent Ethics Committee (IEC) (except where site does not have IRB/IEC according to APPOL and LSOP), except where necessary to eliminate an immediate hazard to the subjects, or where permitted by all applicable regulatory requirements (for example, for administrative aspects of the study).***
- ***That I am thoroughly familiar with the appropriate use of the vaccine, as described in this protocol, and any other information provided by the sponsor, including, but not limited to, the following: the current Investigator's Brochure (IB) or equivalent document, IB supplement (if applicable), prescribing information (in the case of a marketed vaccine).***
- ***That I am aware of, and will comply with, "Good Clinical Practice" (GCP) and all applicable regulatory requirements.***

GlaxoSmithKline Biologicals

Clinical Research & Development

Protocol Amendment

eTrack number and abbreviated title	111700 (Rota-070 PMS)
Title	***S***afety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea. **(Amendment 3: 10 February 2010)**
Detailed Title:	Open, multi-centric, post-marketing surveillance (PMS) to monitor the safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea. **(Amendment 3: 10 February 2010)**
Amendment number:	Amendment 3
Amendment date:	10 February 2010
Co-ordinating author:	PPD Scientific Writer

Rationale/background for changes:
The protocol has been amended to reflect the changes made to the guidelines for Korean New Drug Re-examination by the Korean Food and Drug Administration (KFDA). The current PMS will be conducted as per the local regulatory requirements. Additionally, the protocol reflects the changes in study personnel including the sponsor signatory of the study. The prescribing information has been removed from the protocol.

The changes have been reflected in all applicable sections across the document.

Amended text has been indicated by *bold italics*.

Contributing Authors:

- PPD ***Bio Medical Director, Korea***
- PPD ***Clinical Development Manager, GCRD***
- PPD ***Global Study Manager, GCRD***
- PPD ***Project Leader, Korea***
- PPD ***Medical Advisor, Korea***

Protocol Amendment Sponsor Signatory Approval:

PPD
~~Vice President and Director, Clinical R & D and Medical Affairs, Asia-Pacific, Australasia and China/Hong Kong~~

Dr. PPD
Vice President,
Clinical R&D and Medical Affairs, Asia Pacific

Title Page:
Sponsor:

~~4th Floor, Yeonsei Severance Building 84-11, Namdaemoon-Ro 5-ga, JungGu, Seoul, 100-753, Korea~~

9th Floor LS Yongsan Tower building,
191 Hangang-ro-2-ga, Yongsan-gu,
Seoul, 140-702, Korea

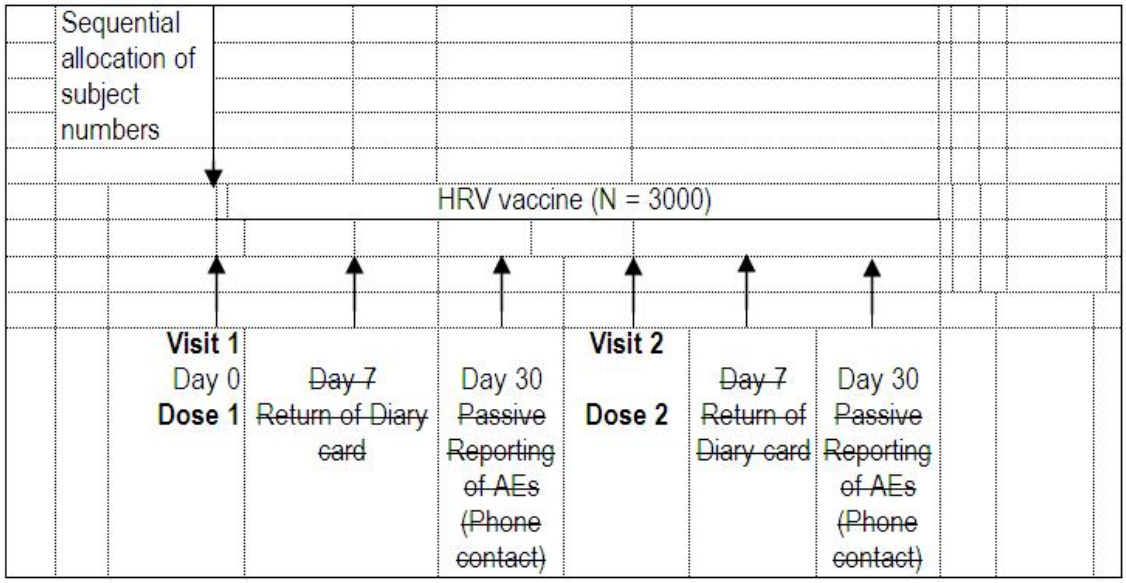
Title:
~~Reactogenicity and S~~afety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.

Detailed Title:
Open, multi-centric, post-marketing surveillance (PMS) to monitor the ~~reactogenicity and~~ safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.

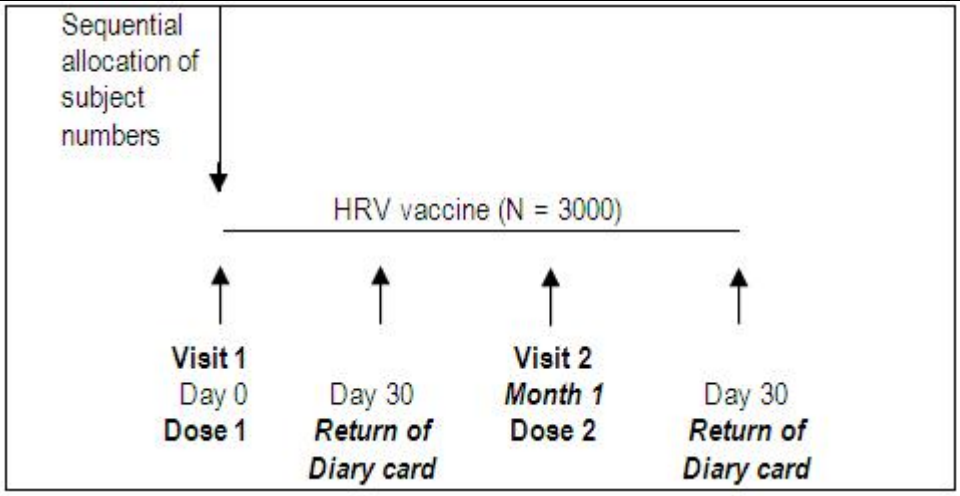
Section 1.2 Rationale for the Post Marketing Surveillance:
GSK Biologicals' vaccine, Rotarix™ was registered in Korea in March 2008, following which, ~~the present PMS will collect reactogenicity and safety data on the use of Rotarix™ in at least 3000 Korean infants as per the regulations of the Korean Food and Drugs Administration (KFDA).~~ ***safety information on the use of Rotarix™ in at least 3000 Korean infants is required as per the regulations of the Korean Food and Drugs Administration (KFDA).***

Section 2. Objectives:
To assess the ~~reactogenicity and~~ safety of Rotarix™ in infants when administered according to the prescribing information in Korea.

Section 3. PMS Design Overview:



~~Approximately 500 subjects will be enrolled every year for 6 years.~~



N: Number of subjects planned to be enrolled.
Infants who have received a dose of the vaccine prior to the start of the PMS will have only one visit followed by the phone contact.
PMS conclusion: An infant's parent/guardian who will be contacted to provide details of any AEs experienced by the infant 30 days after the infant receives the last vaccination or an infant for whom diary card transcription into CRF will be been done through phone contact is considered to have completed the PMS.

- ~~All infants will be followed-up for reactogenicity and safety.~~
- ~~Recording of solicited AEs such as fever, fussiness/irritability, diarrhoea, vomiting, loss of appetite and cough/runny nose from Day 0 to Day 7 after each dose of Rotarix™.~~
- ~~Active~~ ***R***ecording of ~~unsolicited~~ AEs from Day 0 to Day ~~7~~ ***30*** using the diary cards after each dose of Rotarix™. ~~Passive recording of unsolicited symptoms from Day 8 up to Day 30 after each dose of Rotarix™ by phone contact.~~

Section 4.1 Number of subjects/centres:

~~A total of at least 3000 evaluable infants (approximately 500 per year) will be enrolled.~~

As per the KFDA requirements, safety information from a total of 3000 evaluable infants are needed and approximately 500 infants per year will be enrolled.

Section 4.3 Exclusion Criteria for enrolment:

At the time of PMS entry, the contraindications and precautions of use indicated in the prescribing information should be checked and the infant must not be included in the PMS if there is any contraindication. ~~(Refer to Prescribing Information in Appendix C)~~.

Section 4.5 Contraindications to subsequent vaccination:

Refer to the prescribing information for contraindications. ***Any changes in the locally approved Prescribing Information must be implemented immediately.***

Section 4.6 Warnings and Precautions:

Refer to the prescribing information for contraindications. ***Any changes in the locally approved Prescribing Information must be implemented immediately.***

Section 5.1 Ethics and regulatory considerations:

The PMS will be conducted according to ~~Good Clinical Practice (GCP), the Declaration of Helsinki,~~ the local rules and regulations of the country (KFDA) and relevant GSK SOPs/Policies and Guidance.

Submission of the protocol and any protocol amendments to regulatory agencies will occur in accordance with local regulatory requirements ***and relevant GSK SOPs/Policies and Guidance***. If needed, this protocol***/protocol amendment*** will be submitted to ***an*** Institutional Review Board (IRB).

Independent Ethics Committee/Institutional Review Board (IEC/IRB) approval has to be obtained prior to study start. If the regulatory authority and/or IEC/IRB advise that PMS studies do not need ethical review this must be documented. In any event, submission to an IEC/IRB in all institutions where IEC/IRB are available must be carried out and documented.

Section 5.1.1 Informed consent:

In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s) ~~and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki~~.

Freely given informed consent should be obtained from every infants' parents/guardians ~~prior to PMS participation~~ ***for the collection of personal and safety information prior to or post vaccination)***.

An investigator or designate will describe the protocol to potential ~~subjects'~~ ***infants'*** parents/guardians face to face. The Informed Consent Form may be read to the ~~subjects'~~ ***infants'*** parents/guardians, but, in any event, the investigator or designate shall give the ~~subjects'~~ ***infants'*** parents/guardians ample opportunity to inquire about details of the PMS and ask any questions before dating and signing the Informed Consent Form.

Both the informed consent discussion and the written informed consent form and any other written information to be provided to the infants' parents/guardians should include explanations of the following:

j. The approximate number of ~~subjects~~ ***infants*** involved in the PMS.

k. The expected duration of a ~~subject's~~ ***infant's*** participation in the PMS.

Section 5.4 Outline of PMS Procedures:

Age	From the age of 6 weeks					
Visit	**VISIT 1**	~~**Diary Card Return***~~	~~**Passive Reporting**~~ ***Diary Card Return****	**VISIT 2§**	~~**Diary Card Return***~~	~~**Passive Reporting**~~ ***Diary Card Return****
Timing	**Day 0**	~~**Day 7 or after**~~	**Day 30 or after**	**At least 4 weeks after Dose 1**	~~**Day 7 or after**~~	**Day 30 or after**
Informed consent	●					
Check inclusion criteria	●					
Check exclusion criteria	●					
Check contraindications	●			●		
Medical history	●					
Physical examination	●			○		
~~Pre-vaccination~~ ***Recording of*** body temperature	●			●		
Recording of previous Rotarix™ vaccination	●					
Vaccination	●			●		
~~Daily post-vaccination recording of solicited symptoms within 8 days (Days 0 – Day 7) by subjects' parents/guardians on diary cards~~	~~●~~	~~●~~		~~●~~	~~●~~	
Recording of ~~unsolicited symptoms~~ ***AEs*** occurring ~~within 8 days (Day 0 – 7) post-vaccination~~ ***from Day 0 to Day 30 after vaccination***, by ~~subjects~~ ***infants'*** parents/guardians on diary cards	●	~~●~~	●	●	~~●~~	●
~~Passive reporting of unsolicited symptoms occurring from Day 8 up to Day 30 after vaccination~~			~~●~~			~~●~~
Return of diary cards		~~●~~	●		~~●~~	●
Record any concomitant medication/vaccination	●	~~●~~	●	●	~~●~~	●
Reporting of Serious Adverse Events	●	~~●~~	●	●	~~●~~	●
PMS Conclusion			●¶			●

● is used to indicate a PMS procedure that requires documentation in the individual CRF.
○ is used to indicate a PMS procedure that does not require documentation in the individual CRF.
*Diary card will be returned by parents/guardians of infants on Day ~~7~~ ***30*** or after. If the same is not returned, the investigator will make a phone contact to record all AEs in the medical record and then transcribe the information into the CRF.
§Visit 2 will be omitted only for those infants who have received one dose of *Rotarix* prior to the start of the PMS and have received the second dose of the vaccine at Visit 1 or if the investigator confirms that the infant will not be vaccinated in the same centre. The infants who have received a dose of the vaccine prior to the start of the PMS will have only one visit followed by the phone contact and the post-Dose 2 data collected will be recorded under the Visit 2 section of the CRF.
¶If infants receive the 2nd dose at Visit 1 or if the investigator confirms that infants will not be vaccinated in the same centre.

Section 5.5 Detailed description of visits:

Visit 1 (Day 0): Rotarix™ vaccination:

- Checking of contraindications to vaccination ~~(See Appendix C)~~.
- Diary cards will be provided to the parents/guardians of all infants to record information on ~~solicited symptoms (fever, irritability/fussiness, diarrhoea, vomiting, loss of appetite and cough/runny nose) and unsolicited symptoms~~ ***AEs*** occurring on the day of Dose 1 and the following ***30*** days.
- The parents/guardians should be instructed to return the completed diary card to the investigator ~~7~~ ***30*** days following Dose 1, at the next contact or by mail.

~~Day 7 (Return of diary cards/Phone contact)~~

- ~~Recording of solicited symptoms (fever, irritability/fussiness, diarrhoea, vomiting, loss of appetite and cough/runny nose) and unsolicited symptoms occurring from Day 0 – Day 7 after Dose 1.~~
- ~~Diary cards will be filled out by the parents/guardians of all infants and will be returned to the investigator 7 days following Dose 1, at the next contact or by mail. Parents/guardians will be contacted by phone if the investigator does not receive the diary card.~~
- ~~Recording of concomitant medication/vaccination administered in the CRF.~~
- ~~Recording of SAEs.~~
- ~~The investigator will verify the diary card and transcribe the information into the appropriate sections of the CRF, in English.~~

Day 30 (~~Passive Reporting~~ *Return of diary cards*/Phone Contact)

- ~~Passive reporting of unsolicited AEs occurring from Day 8 up to Day 30 after Dose 1 by phone contact.~~
- ***Recording of all AEs occurring from Day 0 – Day 30 after Dose 1.***
- ***Parents/guardians will be contacted by phone if the investigator does not receive the diary cards.***
- ***The investigator will verify the diary card and transcribe the information into the appropriate sections of the CRF, in English.***

Visit 2: *Rotarix* vaccination

- Checking of contraindications to vaccination ~~(See Appendix C)~~.
- Diary cards will be provided to the parents/guardians of all subjects to record information on ~~solicited symptoms (fever, irritability/fussiness, diarrhoea, vomiting, loss of appetite and cough/runny nose) and unsolicited symptoms~~ ***AEs*** occurring on the day of Dose 2 and the following ~~7~~ ***30*** days.
- The parents/guardians should be instructed to return the completed diary card to the investigator ~~7~~ ***30*** days following Dose 2, at the next contact or by mail.

~~**Day 7 after Visit 2(Return of diary cards/Phone contact)**~~

- ~~Recording of solicited symptoms (fever, irritability/fussiness, diarrhoea, vomiting, loss of appetite and cough/runny nose) and unsolicited symptoms occurring from Day 0 – Day 7 after Dose 2.~~
- ~~Diary cards will be filled out by the parents/guardians of all infants and will be returned to the investigator 7 days following Dose 2, at the next contact or by mail. Parents/guardians will be contacted by phone if the investigator does not receive the diary card.~~
- ~~Recording of concomitant medication/vaccination administered in the CRF.~~
- ~~Recording of SAEs.~~
- ~~The investigator will verify the diary card and transcribe the information into the appropriate sections of the CRF, in English~~

Day 30 after Visit 2 (~~Passive Reporting~~ *Return of diary cards/*Phone Contact)

- ~~Passive reporting of unsolicited AEs occurring from Day 8 up to Day 30 after Dose 2 by phone contact.~~
- ***Recording of all AEs occurring from Day 0 – Day 30 after Dose 2.***
- ***Parents/guardians will be contacted by phone if the investigator does not receive the diary cards.***
- ***The investigator will verify the diary card and transcribe the information into the appropriate sections of the CRF, in English.***

Section 6.2 Dosage and administration:

Refer to the prescribing information ~~in Appendix C~~ for details on the dosage and administration of the vaccine.

Section 6.4 Subject number allocation

Target enrolment will be at least 3000 evaluable ~~subjects~~ ***infants*** ~~(approximately 500 subjects per year)~~. ***All infants enrolled into the PMS will receive Rotarix™ vaccine in routine clinical practice settings.***

Section 6.5 Method of blinding and breaking the blind

~~This is an open-label PMS wherein all infants will receive two doses of Rotarix™.~~ ***Not applicable.***

Section 6.9 Concomitant medication/treatment:

All concomitant medication, with the exception of vitamins and/or dietary supplements, administered at ANY time during the period starting with administration of each dose of ~~*Rotarix*~~ ***Rotarix™ after enrolling into the PMS*** up to the end of the follow-up period for ~~unsolicited~~ AEs are to be recorded with generic name of the medication (trade names are allowed for combination drugs, i.e. multi-component drugs), medical indication, total daily dose, route of administration, start and end dates of treatment.

Any vaccine administered in the period beginning 30 days preceding each dose of ~~*Rotarix*~~ ***Rotarix™*** and ending one month (minimum 30 days) after is to be recorded with trade name, route of administration and date(s) of administration.

During the period starting with administration of each dose of ~~*Rotarix*~~ ***Rotarix™*** up to the end of the follow-up period for ~~unsolicited~~ AEs, concomitant medication administered for the treatment of an AE must be recorded in the CRF with generic name of the medication (trade names are allowed for combination drugs only), medical indication (including which AE), total daily dose, route of administration, start and end dates of treatment. Similarly, concomitant medication administered for the treatment of an SAE, at any time, must be recorded on the SAE Report Form.

Section 8.1 Definition of an adverse event:

~~N.B. AEs to be recorded as endpoints (solicited events) are described in Section 8.5.1. All other AEs will be recorded as UNSOLICITED AEs.~~

~~**Solicited adverse events**~~

~~Solicited adverse events will be evaluated within the 8-day (Day 0 – Day 7) follow-up period after each vaccine dose. Diary cards will be provided to the parents/guardians of the subject by the sponsor to record the symptoms observed.~~

~~**Solicited general AEs**~~

~~Table 4 specifies the AEs solicited during this PMS.~~

~~**Table 4 Solicited general adverse events**~~

~~**Fever**~~
~~**Irritability/ Fussiness**~~
~~**Diarrhoea**~~
~~**Vomiting**~~
~~**Loss of appetite**~~
~~**Cough/runny nose**~~

~~N.B. Temperature will be recorded in the evening. Should additional temperature measurements be performed at other times of day, the highest temperature will be recorded.~~

Section 8.5 Time period, frequency, and method of detecting adverse events and serious adverse events

All AEs occurring within 31 days (Day 0 – Day 30) following administration of each dose of vaccine ***received after enrolling into the PMS*** must be recorded into the Adverse Event form in the infant's CRF, irrespective of intensity or whether or not they are considered vaccination-related.

The standard time period for collecting and recording SAEs will begin at the first receipt of ~~Rotarix~~ ***Rotarix™*** and will end at the last contact for each infant.

Section 8.6.1 Assessment of intensity

~~Intensity of the following AEs will be assessed as described in Table 5.~~

Table 5 Intensity scales for solicited symptoms

Adverse Event	Intensity grade	Parameter
Fever*		Record temperature in °C
Irritability/Fussiness	0	Behaviour as usual
	1	Crying more than usual/ no effect on normal activity
	2	Crying more than usual/ interferes with normal activity
	3	Crying that cannot be comforted/ prevents normal activity
Diarrhoea¶		Record the number of looser than normal stools /day
Vomiting§		Record the number of vomiting episodes/day
Loss of appetite	0	Appetite as usual
	1	Eating less than usual/ no effect on normal activity
	2	Eating less than usual/ interferes with normal activity
	3	Not eating at all
Cough/runny nose	0	Normal
	1	Cough/runny nose which is easily tolerated
	2	Cough/runny nose which interferes with daily activity
	3	Cough/runny nose which prevents daily activity

*Fever is defined as: axillary temperature ≥37.5°C/oral temperature ≥37.5°C/tympanic temperature on oral setting ≥37.5°C.
¶Diarrhoea is defined as passage of three or more looser than normal stools within a day.
§Vomiting is defined as one or more episodes of forceful emptying of partially digested stomach contents ≥ 1 hour after feeding within a day.

The maximum intensity of diarrhoea, vomiting and fever occurring during the solicited 8-day (Day 0 – Day 7) follow-up period will be scored at GSK Biologicals as shown in Table 6.

Table 6 Intensity scales used at GSK Biologicals for diarrhoea, vomiting and fever reported during the solicited follow-up period

Adverse Event	Intensity grade	Parameter
Diarrhoea	0	Normal (0 - 2 looser than normal stools/day)
	1	3 looser than normal stools/day
	2	4 - 5 looser than normal stools/day
	3	≥ 6 looser than normal stools/day
Vomiting	0	Normal (no emesis)
	1	1 episode of vomiting/day
	2	2 episodes of vomiting/day
	3	≥ 3 episodes of vomiting/day
Fever	0	tympanic temperature/axillary temperature/oral temperature < 37.5 °C
	1	tympanic temperature/axillary temperature/oral temperature ≥ 37.5 – ≤ 38.0°C
	2	tympanic temperature/axillary temperature/oral temperature > 38.0 – ≤ 39.0°C
	3	tympanic temperature/axillary temperature/oral temperature > 39.0°C

*Fever is defined as: axillary temperature ≥37.5°C/oral temperature ≥37.5°C/tympanic temperature on oral setting ≥37.5°C.

Section 8.6.1 Assessment of Intensity

The investigator will make an assessment of the maximum intensity that occurred over the duration of the event for all other AEs, i.e. unsolicited symptoms~~, including SAEs~~ ***(i.e. non-serious adverse events)*** reported during the PMS.

The intensity of each AE ~~and SAE~~ recorded in the CRF ~~or SAE Report Form~~, as applicable, should be assigned to one of the following categories:

1 (mild)	=	An AE which is easily tolerated by the infant, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE which is sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE which prevents normal, everyday activities. (In a young child, such an AE would, for example, prevent attendance at school/kindergarten/a day-care centre and would cause the parents/guardians to seek medical advice).

An AE that is assessed as Grade "3" (severe) should not be confused with a SAE. Grade "3" is a category utilised for rating the intensity of an event.~~; and both AEs and SAEs can be assessed as Grade "3".~~ An event is defined as 'serious' when it meets one of the pre-defined outcomes as described in Section 8.2.

Section 8.6.2 Assessment of causality

The investigator will also consult the ~~Investigator Brochure and/or~~ Product Information, for marketed products, in the determination of his/her assessment.

As per KFDA requirements, causality will be assessed as:

~~1. Definitely related:~~

- ~~There is evidence of exposure of the drug.~~
- ~~The temporal sequence of the AE onset relative to administration of the drug is reasonable~~
- ~~AE is more likely explained by the drug than by another cause~~
- ~~The AE is subsiding or disappearing on withdrawal of the drug~~
- ~~Rechallenge (if feasible) is positive.~~
- ~~The AE shows a pattern consistent with previous knowledge of the drug or the drug class.~~

~~2. Probably related:~~

- ~~There is evidence of exposure of the drug.~~
- ~~The temporal sequence of the AE onset relative to administration of the drug is reasonable~~
- ~~AE is more likely explained by the drug than by another cause~~
- ~~The AE is subsiding or disappearing on withdrawal of the drug~~

~~3. Possibly related:~~

- ~~There is evidence of exposure of the drug.~~
- ~~The temporal sequence of the AE onset relative to administration of the drug is reasonable~~
- ~~The AE could have been due to another equally likely cause~~
- ~~The AE is subsiding or disappearing on withdrawal of the drug (if performed)~~

~~4. Probably not related:~~

- ~~There is no evidence of exposure of the drug~~
- ~~There is another more likely cause of the AE~~
- ~~The AE is not disappearing even on withdrawal of the drug (if performed) or ambiguous~~

5. ~~Unknown~~

NOTE: The use of the term "drug" here refers to the vaccine.

As per KFDA requirements, causality will be assessed as:

1. ***Certain:***
   - ***The relationship of the administration and use of the drug is reasonable and it is not able to be explained by other medication, chemical substances or concomitant disease, it shows clinically reasonable response on withdrawal of the drug, the decisive case in the pharmacological or phenomenological aspect on re-challenge of the drugs if needed.***
2. ***Probable/Likely:***
   - ***The temporal sequence of the administration and use of the drug is appropriate and it does not seem that it is accompanied by other medications, chemical substances or concomitant disease, in the case that shows clinically appropriate response on withdrawal of the drug (no information for re-challenge).***
3. ***Possible:***
   - ***The temporal sequence of the administration and use of the drug is appropriate but it is also able to be explained by other medications, chemical substances or concomitant disease, and information related to withdrawal of the drug is insufficient or vague.***
4. ***Unlikely:***
   - ***It is a transitory case which may not have causality with the administration and use of the drug, it is also able to be explained reasonably by other medications, chemical substances or latent disease.***
5. ***Conditional/Unclassified:***
   - ***In the case that more information is needed for a proper evaluation or additional information is under review.***
6. ***Unassessible/Unclassifiable:***
   - ***In the case that could not be judged due to insufficient or conflicting information and no way to complement or validate.***

Section 8.6.3 Medically attended visits

For each ~~solicited and unsolicited symptom~~ ***AE*** the infant experiences, the infant's parents/guardians will be asked if they received medical attention defined as hospitalisation, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information will be recorded in the CRF.

Section 8.7 Follow-up of adverse events and serious adverse events and assessment of outcome

Outcome of any non-serious AE occurring within 31 days (Day 0 – Day 30) days post-vaccination ~~(i.e. unsolicited AE)~~ or any SAE reported during the entire PMS will be assessed as:

- Recovered/resolved
- Not recovered/not resolved
- Recovering/resolving
- Recovered with sequelae/resolved with sequelae
- Fatal (SAEs only)
- ***Unknown***

Section 8.8.2. Completion and transmission of serious adverse event reports to GSK Biologicals

~~**Study Contact for Reporting SAEs**~~
~~Refer to the Sponsor Information Sheet~~
~~**Back-up Study Contact for Reporting SAEs**~~
~~**GSK Biologicals Clinical Safety Physician**~~ ~~Tel:~~ PPD ~~Fax:~~ PPD ~~or~~ PPD ~~Mobile phones for 7/7 day availability:~~ PPD ~~(Head Safety Evaluation and Risk Management Paediatric)~~ ~~Back-up mobile phone contact:~~ PPD PPD ~~**24/24 hour and 7/7 day availability**~~

Study Contact for Reporting SAEs
Refer to the Sponsor Information Sheet
Back-up Study Contact for Reporting SAEs
GSK Biologicals Clinical Safety *and Pharmacovigilance* Fax: PPD or PPD **24/24 hour and 7/7 day availability**
Section 8.10 Post-PMS adverse events and serious adverse events However, if the investigator learns of any SAE, including a death, at any time after an infant has been discharged from the PMS, and he/she considers the event reasonably related to ~~*Rotarix*~~ ***Rotarix™***, the investigator will promptly notify the Study Contact for Reporting SAEs. **Section 9.1 Subject completion** An infant who has the 30 day safety contact ~~for passive reporting~~ after the second Rotarix™ vaccination is considered to have completed the PMS.
Section 9.2.1 Subject withdrawal from the PMS A subject qualifies as a 'withdrawal' from the PMS if the second Rotarix™ vaccination is not given in this PMS or when the 30 day safety contact ~~for passive reporting~~ after the last Rotarix™ dose does not take place.
Section 10.1 Endpoints • ~~Occurrence of solicited AEs during the 8-day (Day 0 – Day 7) follow-up after each vaccine dose.~~ • Occurrence of ~~unsolicited~~ AEs during the 31-day (Day 0 – Day 30) follow-up period after each vaccine dose according to Medical Dictionary for Regulatory Activities (MedDRA) classification.
Section 10.3.1 Total Vaccinated Cohort The total vaccinated cohort will include all vaccinated subjects with at least one dose of ~~Rotarix~~ **Rotarix™** administration documented **Section 10.4 Derived and transformed data** Infants who missed reporting symptoms (~~solicited/unsolicited~~ ***AEs*** or concomitant medications) will be treated as ~~withdrawals~~ ***infants without symptoms*** (~~solicited/unsolicited~~ ***AEs*** or concomitant medications, respectively).

Section 10.5 Final analyses

Statistical analyses will be performed as per the GSK standards as well as to reflect the requirements of KFDA.

Section 10.5.2 Analysis of safety

For all infants enrolled prior to Amendment 3 dated 10 February 2010, the following statistical analysis will be performed:

For all subjects enrolled after the Amendment 3 dated 10 February 2010, the following statistical analysis will be performed:

The AEs/SAEs collected will be analysed in the study report according to the expectedness and unexpectedness criteria. Refer to the Glossary of Terms for the definitions of expected AEs and unexpected AEs.

The overall incidence, with exact 95% confidence interval (CI), of any adverse events occurring within 31 days will be tabulated, for each dose, for overall doses and per subject. The same calculations will be done for any adverse events; rated as grade "3" and for all the causality grading mandated by KFDA.

The verbatim reports of AEs will be reviewed by a physician and the signs and symptoms will be coded according to MedDRA. Every verbatim term will be matched with the appropriate Preferred Term. The percentage of subjects with AEs occurring within 31 days with its exact 95% CI will be tabulated by preferred term. Similar tabulation will be done for AEs rated as grade 3 and for all causality grading mandated by KFDA.

The percentage of subjects who received at least one concomitant medication/vaccination during the 30 day follow-up period will be tabulated by type of medication, with exact 95% CI. Similar tabulations will be done for subjects who receive concomitant medication/vaccination during the entire PMS period.

Serious adverse events and withdrawals due to adverse events reported during the PMS period will be described in detail.

In addition, specific statistical analyses (e.g. AEs classified by gender, past medical history, concomitant medication/vaccination etc) will be performed to reflect the KFDA requirements.

Section 11 Administrative Matters

To comply with ~~Good Clinical Practice,~~ local rules, regulations, relevant GSK SOPs/Policies/Guidance, important administrative obligations relating to investigator responsibilities, monitoring, archiving data, audits, confidentiality and publications must be fulfilled.

Appendix A Administrative Matters

Responsibilities of the Investigator

- To conduct the study in compliance with the protocol any amendment***,*** ~~and~~ ~~"Good Clinical Practice" (GCP) and~~ all applicable regulatory requirements ***and GSK SOPs/Policies and Guidance.***

Monitoring by GSK Biologicals

- These visits are for the purpose of confirming that GSK Biologicals' sponsored studies are being conducted in accordance with the ethical principles ~~that have their origins in the Declaration of Helsinki and that are consistent with Good Clinical practice (GCP)~~, the applicable regulatory requirement(s) and relevant GSK SOPs/Policies and Guidance (verifying continuing compliance with the protocol, amendment(s), verifying that the site staff and facilities continue to be adequate to conduct the PMS.

Audits

- For the purpose of compliance with ~~Good Clinical Practice,~~ Regulatory Agency Guidelines and relevant GSK SOPs/Policies and Guidance it may be necessary for GSK or a Drug Regulatory Agency to conduct a site audit.
- In addition, Regulatory Compliance assures that GSK Biologicals' sponsored studies are in accordance with ~~GCP and that~~ relevant ***regulatory***/guidelines and relevant GSK SOPs/Policies and Guidance are being followed

Appendix B Overview of Recruitment Plan:

- Target enrolment will be at least 3000 evaluable ~~subjects~~ ***infants*** ~~(approximately 500 subjects per year)~~
- ***The PMS is required to be conducted in at least one hospital (with IRB oversight) in order for PMS to be conducted in private clinics (with no IRB).***

Appendix C Prescribing Information

Refer to locally approved prescribing information. (The prescribing information has been deleted from the protocol).

GlaxoSmithKline Biologicals

Clinical Research & Development

Protocol Amendment 4

eTrack study number and Abbreviated Title	111700 (Rota-070 PMS)
Amendment number:	Amendment 4
Amendment date:	23 February 2012
Co-ordinating author:	PPD Project Manager - Scientific Writing, Manpower Business Solutions for GSK Biologicals.

Rationale/background for changes:
The protocol has been amended to reflect the two new vaccine presentations that have been launched in Korea. The current PMS will thus collect safety information from subjects who have received either Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe).

The changes have been reflected in all applicable sections across the document.
Amended text has been indicated by *bold italics*.

Title Page:
GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***

Title:
Safety of GlaxoSmithKline ~~(GSK)~~ Biologicals' oral live attenuated human rotavirus ~~(HRV)~~ vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea.

Detailed Title:
Open, multi-centric, post-marketing surveillance (PMS) to monitor the safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea.

Section 1.2 Rationale:
GSK Biologicals' vaccine, Rotarix™ ***(lyophilised formulation)*** was registered in Korea in March 2008. ***Rotarix™ liquid formulation (oral suspension) was registered in Korea in January 2011 while Rotarix™ liquid formulation (prefilled syringe) was registered in December 2011. Following the vaccine registration***, safety information on the use of ***all the Rotarix™ presentations*** is required as per the regulations of the Korean Food and Drugs Administration (KFDA) in at least 3000 ***evaluable*** Korean infants.

Section 2 Objective:
To assess the safety of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** in infants when administered according to the prescribing information in Korea.

Section 3 PMS Design:

- Vaccination schedule: Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be administered orally as per the prescribing information in Korea.

Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** should be given before 24 weeks of age.

- Two visits are recommended as follows:
  - Visit 1: Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination, subjects will be allowed to receive concomitant vaccinations.
  - Visit 2: Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination, subjects will be allowed to receive concomitant vaccinations.
- Recording of AEs from Day 0 to Day 30 using the diary card after each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***.

Section 4.1 Number of Subjects:
As per the KFDA requirements, safety information from at least 3000 evaluable infants are needed ***for this PMS study***.

Section 4.2 Inclusion Criteria:

- A male or female infant from the age of 6 weeks at the time of the first vaccination. (Note: Two doses of the Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccine should be completed by the age of 24 weeks).

Footnote for Table 1 List of PMS procedures:
§Visit 2 will be omitted only for those infants who have received one dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** prior to the start of the PMS and have received the second dose of the vaccine at Visit 1 or if the investigator confirms that the infant will not be vaccinated in the same centre.

Section 5.5 Detailed description of visits:
Visit 1 (Day 0): Rotarix™ *or Rotarix™ liquid formulation (oral suspension or prefilled syringe)* vaccination

- Record previous history of any Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccine administration (if applicable)
- Vaccination:
  - One dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be administered orally according to instructions specified in section 6.2.

Visit 2: Rotarix™ *or Rotarix™ liquid formulation (oral suspension or prefilled syringe)* vaccination

- Vaccination:
  - One dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be administered orally according to instructions specified in section 6.2.

Section 6 Indication and Dosage/Administration
Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***to be used in this PMS has been developed and manufactured by GSK Biologicals.

Section 6.2 Dosage and administration
Rotarix™ ***or Rotarix™ liquid formulation (oral suspension) or Rotarix™ liquid formulation (prefilled syringe)*** will be administered twice orally as per the prescribing information in Korea.

Two doses of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** should be given before 24 weeks of age.

Section 6.4 Subject number allocation
Target enrolment will be at least 3000 evaluable infants. All infants enrolled into the PMS will receive Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccine in routine clinical practice settings.

Section 6.9 Concomitant medication/treatment

All concomitant medication, with the exception of vitamins and/or dietary supplements, administered at ANY time during the period starting with administration of each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** after enrolling into the PMS up to the end of the follow-up period for AEs are to be recorded with generic name of the medication (trade names are allowed for combination drugs, i.e. multi-component drugs), medical indication, total daily dose, route of administration, start and end dates of treatment.

Any vaccine administered in the period beginning 30 days preceding each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** and ending one month (minimum 30 days) after is to be recorded with trade name, route of administration and date(s) of administration.

During the period starting with administration of each dose of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** up to the end of the follow-up period for AEs, concomitant medication administered for the treatment of an AE must be recorded in the CRF with generic name of the medication (trade names are allowed for combination drugs only), medical indication (including which AE), total daily dose, route of administration, start and end dates of treatment.

Section 8.2 Definition of a serious adverse event

- ~~Is a congenital anomaly/birth defect in the off spring of a subject.~~

Section 8.5 Time period, frequency and method of detecting adverse events and serious adverse events

The standard time period for collecting and recording SAEs will begin at the first receipt of ***Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** and will end at the last contact for each infant.

Section 8.6.2 Assessment of causality

The investigator is obligated to assess the relationship between Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** and the occurrence of each AE/SAE. The investigator will use clinical judgement to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors and the temporal relationship of the event to Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be considered and investigated. The investigator will also consult the Product Information, for marketed products, in the determination of his/her assessment.

Causality of all AEs should be assessed by the investigator using the following question:

Is there a reasonable possibility that the AE may have been caused by Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***?

Section 8.10 Post PMS adverse events and serious adverse events
However, if the investigator learns of any SAE, including a death, at any time after an infant has been discharged from the PMS, and he/she considers the event reasonably related to Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)***, the investigator will promptly notify the Study Contact for Reporting SAEs.

Section 9.1 Subject completion
An infant who has the 30 day safety contact after the second Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination is considered to have completed the PMS.

Section 9.2.1 Subject withdrawal from the PMS
A subject qualifies as a 'withdrawal' from the PMS if the second Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** vaccination is not given in this PMS or when the 30 day safety contact after the last Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** dose does not take place.

Section 9.2.2 Subject withdrawal from Rotarix
A 'withdrawal' from Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** is any infant who does not receive the second Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** dose in the PMS. An infant withdrawn from Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** may not necessarily be withdrawn from the PMS as further procedures or follow-up may be performed (safety) if planned in the protocol.

Information relative to premature discontinuation of Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** will be documented on the Vaccine Administration page of the CRF.

Section 10.2 Estimated sample size
According to KFDA regulation requirement, at least 3000 evaluable subjects ~~(approximately 500 subjects per year for a period of 6 consecutive years)~~ will be recruited for the PMS.

~~Table 4 and~~ Table 5 present***s*** the exact two-sided 95% confidence interval for a sample size of ~~500 (~~3000~~)~~ subjects.
~~**Exact two-sided 95% CI for a sample size of 500 subjects**~~

~~Observed rate expressed as a percentage (number of subjects reporting at least one symptom)~~	~~Exact two-sided 95% CI for this observed rate for a sample size of 500 subjects~~	
	~~Lower limit (LL)~~	~~Upper limit (UL)~~
~~50(250)~~	~~45.5~~	~~54.5~~
~~55(275)~~	~~50.5~~	~~59.4~~
~~60(300)~~	~~55.6~~	~~64.3~~
~~65(325)~~	~~60.6~~	~~69.2~~
~~70(350)~~	~~65.8~~	~~74.0~~
~~75(375)~~	~~71.0~~	~~78.7~~
~~80(400)~~	~~76.2~~	~~83.4~~
~~85(425)~~	~~81.6~~	~~88.0~~

Section 10.3.1 Total Vaccinated Cohort

The total vaccinated cohort will include all vaccinated subjects with at least one dose of ***Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** administration documented.

Study Reporting and Analysis Plan Approval

Title:	Open, multi-centric, post-marketing surveillance (PMS) to monitor the reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals. oral live attenuated human rotavirus (HRV) vaccine, Rotarix. When administered according to the prescribing information in Korea
eTrack study number	111700
eTrack abbreviated title	Rota-070 PMS
Scope:	All data pertaining to the above study
Date:	19-Jan-2009
Co-ordinating author:	PPD
Other author(s):	PPD

Approved by:

Director, Global Clinical Research and Development			
	Name	Signature	dd-mmm-yyyy
	PPD		
Clinical Development Manager			
	Name	Signature	dd-mmm-yyyy
	PPD		
Project Statistician			
	Name	Signature	dd-mmm-yyyy
	PPD		
Franchise Statistician	Name	Signature	dd-mmm-yyyy
	PPD		

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LIST OF ABBREVIATIONS

AE	Adverse event
CI	Confidence Interval
CRF	Case Report Form
GSK	GlaxoSmithKline
MedDRA	Medical Dictionary for Regulatory Activities
NA.	Not Applicable
GE	Gastroenteritis
SAE	Serious Adverse Event
HRV	Human rotavirus
LL	Lower limit
UL	Upper limit
SD	Standard deviation

1. LIST OF AMENDMENTS TO THE RAP

Date	Description
19 Jan 2009	First version

2. INTRODUCTION

This document summarizes the planned statistical analyses (Sections 3 & 4) based on the study features as per protocol amendment 2 dated 13Oct2008. The changes in the analyses as compared to the protocol/amendment 2 are provided in section 4. The list of tables/listings to be produced in the statistical report is available in section 5.

3. DATA EVALUATION: CRITERIA FOR EVALUATION OF OBJECTIVES

3.1. Endpoints

- Occurrence of solicited AEs during the 8-day (Day 0 – Day 7) follow-up after each vaccine dose.
- Occurrence of unsolicited AEs during the 31-day (Day 0 – Day 30) follow-up period after each vaccine dose according to Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of SAEs during the entire PMS period..

3.2. Study cohorts to be evaluated

Total Vaccinated cohort

The total vaccinated cohort will include all vaccinated subjects with at least one dose of Rotarix administration documented:

- a safety analysis based on the total vaccinated cohort will include all vaccinated subjects.

The list of applicable elimination codes for each cohort can be found in the study specific form FORM-BIO-WWCD-9004-05 Elim code specifications.

Cohort	Elimination codes	Eli Type
Total vaccinated cohort	1030	MA

3.3. Derived and transformed data

Infants who missed reporting symptoms (solicited/unsolicited or concomitant medications) will be treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively). In case of significant non-compliance of PMS procedures for reporting symptoms, the analysis plan will be reassessed to ensure more accurate reporting of PMS data by further analysis.

3.4. Data presentation description

The following decimal description will be used for the demography, reactogenicity/Safety.

Display Table	Parameters	Number of decimal digits
All summaries	% of count, including LL & UL of CI	1
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	2

3.5. Group description

The following group will be used for the statistical analyses.

Study	Group order in tables	Group label in tables
Rota_070	1	HRV

3.6. Final analyses

As per protocol.

3.7. Methodology for computing CI

All CI will be 2 sided 95% CI.

- The exact 95% CIs for proportion within a group will be calculated from Proc StatXact 7.0 assuming independence between doses.

3.8. Conduct of analyses

3.8.1. Sequence of analyses

NA

3.8.2. Statistical considerations for interim analyses

As per protocol

3.9. Statistical methods

As per protocol

4. CHANGE FROM PROTOCOL

- **Derived and Transformed Data**: Infants who missed reporting symptoms (solicited/unsolicited or concomitant medications) will be treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

- A combined year1 & 2 analyses will be performed for this time point.

- KFDA Specific tables and Listings are mentioned in RAP

5. ANNEX 1: INDIVIDUAL LISTINGS AND TEMPLATE OF TABLES

5.1. Individual listings

Appendix Table I.A - Elimination codes

Appendix Table I.B - Demography

Appendix Table I.Ci - Dates of birth, Informed consent, Vaccination and Contact

Appendix Table I.Cii - Reason for visit not done

Appendix Table I.G - Vaccination procedure

Appendix Table I.H - Previous History of Rotavirus Vaccination

Appendix Table I.I - Reason for not administration of vaccine

Appendix Table II.B - Solicited general symptoms

Appendix Table II.Ci - Unsolicited adverse events

Appendix Table II.Di - Concomitant medications

Appendix Table II.Dii - Concomitant vaccinations

Appendix table I E - Study Conclusion

5.2. List of tables

5.2.1. For Demographics & baseline characteristics Analysis:

TABLE # in reference of section 5.3	Table Title	Analysis year 1 & year 2	Macro
Table D 1	Number of subjects enrolled into the study as well as the number of subjects excluded with reasons for exclusion.	CR	%ELIMLIST
Table D 2	Number of subjects by center (Total vaccinated cohort)	CR	%CENTER
Table D 3	Number of subjects at each visit and list of withdrawn subjects (Total vaccinated cohort)	ST	%DROPOUT
Table D 4	Number of subjects entered, completed and withdrawn with reason for withdrawal (Total vaccinated cohort)	CR	%DROP_SUM
Table D 5	Minimum and maximum activity dates (Total vaccinated cohort)	WT	%DATE
Table D 6	Summary of demographic characteristics (Total vaccinated cohort)	CR	%DEMOGRA
Table D 7	Summary of Previous rotavirus vaccination history (Total vaccinated cohort)	CR	%FREQ_DIS
Table CTRS 1	Demography for CTRS	CTRS	%CTR_DEMOG

CR = Within the clinical report
ST = As a supplementary table or figure
WT = As a working or CTRS table or figure

5.2.2. For Reactogenicity Analysis:

TABLE # in reference of section 5.3	Table Title	Analysis year 1 & year 2	Macro
Table R 1	Number and percentage of subjects who received vaccine dose(s) (Total vaccinated cohort)	CR	%EXPO
Table R 2	Compliance in returning symptom sheets (Total Vaccinated Cohort)	ST	%COMPLI
Table R 3	Percentage of doses and of subjects reporting symptoms (solicited or unsolicited) during the 8-day (Days 0-7) solicited follow-up period (Total vaccinated cohort)	CR	%LOCGEN
Table R 4	Percentage of doses and of subjects reporting grade 3 symptoms (solicited or unsolicited) during the 8-day (Days 0-7) solicited follow-up period (Total vaccinated cohort)	CR	%LOCGEN
Table R 5	Percentage of doses and of subjects reporting symptoms assessed as related to vaccination (solicited or unsolicited) during the 8 day (Days 0-7) solicited follow-up period (Total vaccinated cohort)	CR	%LOCGEN
Table R 6	Percentage of subjects reporting each solicited general symptom including those graded 3 in intensity and those assessed as related to vaccination during the 8-day (Days 0-7) solicited follow-up period, for each dose (Total vaccinated cohort)	CR	%FREQ
Table R 7	Percentage of doses and subjects reporting each solicited general symptom including those graded 2 or 3 in intensity and those assessed as related to vaccination during the 8-day (Days 0-7) solicited follow-up period, for all doses and per subject (Total vaccinated cohort)	ST	%FREQ
Table R 8	Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)	CR	%UNSOL
Table R 9	Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)	ST	%UNSOL
Table R 10	Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term	CR	%UNSOL

TABLE # in reference of section 5.3	Table Title	Analysis year 1 & year 2	Macro
	within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)		
Table R 11	Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)	ST	%UNSOL
Table R 12	Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term that are causally related to vaccination, within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)	CR	%UNSOL
Table R 13	Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term that are causally related to vaccination, within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)	ST	%UNSOL
Table R 14	Percentage of subjects reporting the occurrence of unsolicited symptoms leading to drop out during the study period (Total vaccinated cohort)	ST	%UNSOL
Table R 15	Percentage of doses with unsolicited symptoms leading to drop out during the study period (Total vaccinated cohort)	ST	%UNSOL
Table R 16	Listing of SAEs	ST	%SAE
Table R 17	Number and percentage of doses and of subjects who took at least one concomitant medication from Day 0 to Day 7 after vaccination by type (Total vaccinated cohort)	CR	%CMED_INC
Table R 18	Number and percentage of doses and of subjects who took at least one concomitant medication during the entire study period by dose and overall (Total vaccinated cohort)	ST	%CMED_INC
Table CTRS 2	Number (%) of subjects with solicited general symptom during the 8-day (Days 0-7) post-vaccination period (Total Vaccinated Cohort)	CTRS	%FREQ
Table CTRS 3	Number (%) of subjects with adverse events (Total vaccinated cohort)	CTRS	%CTR_AE
Table CTRS 4	Number (%) of subjects with serious adverse events (Total vaccinated cohort)	CTRS	%CTR_SAE

CR = Within the clinical report
ST = As a supplementary table or figure
WT = As a working table or figure

5.2.3. KFDA specific listings

TABLE # in reference of section 5.3	Title
Table KFDA 1	Summary of post marketing surveillance
Table KFDA 2	Table of Subjects
Table KFDA 3	Line-listing of AE
Table KFDA 4	Line-Listing of Adverse Events with a causal relationship to vaccination.
Table KFDA 5	Line-listing AEs from clinical trial and spontaneous report
Table KFDA 6	Line-listing of reported SAE and unexpected ADR
Table KFDA 7	Contents of SAE and unexpected ADR
Table KFDA 8	Table KFDA 8 Line-listing of SAE and unexpected ADR
Table KFDA 9	Individual Line-listing for All Subjects

5.2.4. KFDA specific tables

TABLE # in reference of section 5.3	Title
Table KFDA 10	Demographic data - by gender
Table KFDA 11	Pre-exist medical history – by gender
Table KFDA 12	pre-exist medical history - by classification
Table KFDA 13	Pre-rotavirus vaccination history
Table KFDA 14	Administration of concomitant medication – by gender
Table KFDA 15	Administration of concomitant medication – by classification
Table KFDA 16	Administration of concomitant vaccination
Table KFDA 17	Administration of study vaccination – by gender
Table KFDA 18	Summary of serious adverse events, adverse drug reactions
Table KFDA 19	Serious adverse events, adverse drug reactions
Table KFDA 20	Adverse events, adverse drug reactions
Table KFDA 21	Adverse events (Solicited and Unsolicited) experienced by subjects during the entire study period; stratified by age (Total vaccinated cohort)
Table KFDA 22	Adverse events (Solicited and Unsolicited) experienced by subjects during the entire study period; stratified by age (Total vaccinated cohort)
Table KFDA 23	Adverse events (Solicited and Unsolicited) experienced by subjects at any time during the study; stratified by concomitant medication (Total vaccinated cohort)
Table KFDA 24	Adverse events (Solicited and Unsolicited) experienced by subjects at any time during the study; stratified by concomitant vaccination (Total vaccinated cohort)
Table KFDA 25	Adverse events experienced by subjects at any time during the study; stratified by past medical history status (Total vaccinated cohort)
Table KFDA 26	Adverse events by medical history – by gender & classification
Table KFDA 27	Adverse events by concomitant medication – by classification
Table KFDA 28	Adverse events by concomitant vaccinations – by Classification
Table KFDA 29	Adverse events by medical history, Concomitant vaccination, concomitant medication

Table KFDA 30	Adverse events by duration
Table KFDA 31	Adverse events by severity
Table KFDA 32	Adverse events by causality
Table KFDA 33	Adverse events by outcome

- Tables KFDA 5,6,8 will be generated by LOC

5.3. Template of tables

The following tables/figures provide lay-out tables for the statistical analyses

Table D 1 Number of subjects enrolled into the study as well as the number of subjects excluded with reasons for exclusion.

	HRV		
Title	**n**	**s**	**%**
Total enrolled cohort	xxx		
Study vaccine dose not administered AT ALL but subject number allocated (code 1030)	xx	xx	
Total vaccinated cohort	xxx		xxx

n= number of subjects eliminated under the respective code
s= number of subjects with the elimination code assigned

Table D 2 Number of subjects by center (Total vaccinated cohort)

Center	HRV	
	n	%
PPD		
All		

- n = number of subjects included in the group for a given center or for all centers.
- All = sum of all subjects in the group (sum of all center).
- % = n/All*100
- Center = GSK assigned center number.

Table D 3 Number of subjects at each visit and list of withdrawn subjects (Total vaccinated cohort)

Visit	N	Withdrawn Subject	Reasons for withdraw
Visit1			
Visit2			

N = number of subjects in the vaccine group

Table D 4 Number of subjects entered, completed and withdrawn with reason for withdrawal (Total vaccinated cohort)

	HRV
Number of subjects enrolled	
Number of subjects completed	
Number of subjects withdrawn	
Reasons for withdraw:	
Serious Adverse Event	
Non-serious adverse event	
Protocol violation	
Consent withdrawal (not due to an adverse event)	
Migrated/moved from study area	
Lost to follow-up (subjects with incomplete vaccination course)	
Lost to follow-up (subjects with complete vaccination course)	
Others	

Enrolled = number of subjects who were enrolled in the study
Completed = number of subjects who completed the study
withdrawn = number of subjects who did not come to concluding visit

Table D 5 Minimum and maximum activity dates (Total vaccinated cohort)

Activity number	Description of the Activity	Minimum date	Maximum date
10	Visit 1		
20	Visit 2		

Table D 6 Summary of demographic characteristics (Total vaccinated cohort)

Characteristics	Parameters or Categories	HRV N= XXX	
		Value or n	%
Age(W) at Dose 1 of HRV *	Mean SD Median Minimum Maximum		
Age(W) at Dose 2 of HRV	Mean		
	SD		
	Median		
	Minimum		
	Maximum		
Gender	Female Male		
Race	Korean Other		

N = total number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n / Number of subjects with available results x 100
SD= standard deviation
Age(W)= age expressed in Weeks
* = For those subjects who received the first dose of HRV outside the PMS study, age at dose 1 is computed considering the approximate date of vaccination coded in the CRF.

Table D 7 Summary of Previous rotavirus vaccination history (Total vaccinated cohort)

		HRV N= XXX	
Characteristics	**Parameters or Categories**	**n**	**%**
Did the subject receive HRV vaccine prior to the PMS study?	**Yes**		
	No		

N = Total number of subjects
n = number of subjects with HRV vaccination prior to start of this study
% = n / Number of subjects with available results x 10
Yes: Subjects with a dose of HRV prior to start of the PMS study
No: Subjects who received both the doses in this PMS study

Table R 1 Number and percentage of subjects who received vaccine dose(s) (Total vaccinated cohort)

Total number of doses received	HRV (N = XXX)	
	n	%
1		
2		
Any		

N = number of subjects in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose

Table R 2 Compliance in returning symptom sheets (Total Vaccinated Cohort)

Number of Doses	Group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % General SS
1	HRV				
2	HRV				

SS = Symptom sheets used for the collection of general solicited AEs
Compliance % = (number of subjects returning a symptom sheet (SS)/number of doses) x 100

Table R 3 Percentage of doses and of subjects reporting symptoms (solicited or unsolicited) during the 8-day (Days 0-7) solicited follow-up period (Total vaccinated cohort)

		Any symptom				
					95% CI	
	Group	N	n	%	LL	UL
Dose 1	HRV					
Dose 2	HRV					
Overall/dose	HRV					
Overall/subject	HRV					

For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table R 4 Percentage of doses and of subjects reporting grade 3 symptoms (solicited or unsolicited) during the 8-day (Days 0-7) solicited follow-up period (Total vaccinated cohort)

See template for **Table R 3**

Table R 5 Percentage of doses and of subjects reporting symptoms assessed as related to vaccination (solicited or unsolicited) during the 8 day (Days 0-7) solicited follow-up period (Total vaccinated cohort)

See template for **Table R 3**

Table R 6 Percentage of subjects reporting each solicited general symptom including those graded 3 in intensity and those assessed as related to vaccination during the 8-day (Days 0-7) solicited follow-up period, for each dose (Total vaccinated cohort)

		HRV				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1						
Cough /Runny nose	All					
	Grade 3					
	Related					
Diarrhoea	All					
	Grade 3					
	Related					
Fever/(Axillary) (°C)	All					
	Grade 3					
	Related					
Irritability	All					
	Grade 3					
	Related					
Loss of appetite	All					
	Grade 3					
	Related					
Vomiting	All					
	Grade 3					
	Related					
Dose 2						
Cough /Runny nose	All					
	Grade 3					
	Related					
Diarrhoea	All					
	Grade 3					
	Related					
Fever/(Axillary) (°C)	All					
	Grade 3					
	Related					
Irritability	All					
	Grade 3					
	Related					
Loss of appetite	All					
	Grade 3					
	Related					
Vomiting	All					
	Grade 3					
	Related					

For each dose:

N= number of subjects with at least one administered dose
n/%= number/percentage of subjects reporting at least once the symptom

Table R 7 Percentage of doses and subjects reporting each solicited general symptom including those graded 2 or 3 in intensity and those assessed as related to vaccination during the 8-day (Days 0-7) solicited follow-up period, for all doses and per subject (Total vaccinated cohort)

		HRV				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject						
Cough /Runny nose	All					
	Grade 3					
	Related					
Diarrhoea	All					
	Grade 3					
	Related					
Fever/(Axillary) (°C)	All					
	Grade 3					
	Related					
Irritability	All					
	Grade 3					
	Related					
Loss of appetite	All					
	Grade 3					
	Related					
Vomiting	All					
	Grade 3					
	Related					
Overall/dose						
Cough /Runny nose	All					
	Grade 3					
	Related					
Diarrhoea	All					
	Grade 3					
	Related					
Fever/(Axillary) (°C)	All					
	Grade 3					
	Related					
Irritability	All					
	Grade 3					
	Related					
Loss of appetite	All					
	Grade 3					
	Related					
Vomiting	All					
	Grade 3					
	Related					

Overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects reporting at least once the symptom
For Overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom

Table R 8 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)

Primary System Organ Class (CODE)	Preferred Term (CODE)	HRV			
		n	%	95% CI	
				LL	UL
At least one symptom	Any				
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)				
Autonomic nervous (420)	Mouth dry (0218)				
Body as a whole	Allergy (1058)				
general (1810)	Chest pain (0718)				
	Fever (0725)				
	Influenza-like symptoms (1222)				
	Injury (9001)				
	Pain (0730)				
……					

At least one symptom = At least one symptom experienced regardless of the System Organ Class
N = Number of subjects having received at least one dose
n/% = Number / percentage of subjects reporting at least once a specified symptom within 31 days after vaccination day 0 to day 30
95% CI = Exact 95% confidence interval

Table R 9 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)

		HRV (N=xxx)			
				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**
At least one symptom					
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)				
	Iron deficiency anaemia (10022972)				
	Lymphadenitis (10025188)				
Ear and labyrinth disorders (10013993)	Hearing impaired (10019245)				
	Otorrhoea (10033101)				
Eye disorders (10015919)	Conjunctivitis (10010741)				
	Eye swelling (10015967)				
General disorders and administration site conditions (10018065)	Cyst (10011732)				
	Developmental delay (10012559)				
……					

At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table R 10 Percentage of subjects reporting the occurrence of grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)

See template for **Table R 8**

Table R 11 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)

See template for **Table R 9**

Table R 12 Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term that are causally related to vaccination, within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)

See template for **Table R 8**

Table R 13 Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term that are causally related to vaccination, within the 31-day (Days 0-30) post-vaccination period (Total vaccinated cohort)

See template for **Table R 9**

Table R 14 Percentage of subjects reporting the occurrence of unsolicited symptoms leading to drop out during the study period (Total vaccinated cohort)

See template for **Table R 8**

Table R 15 Percentage of doses with unsolicited symptoms leading to drop out during the study period (Total vaccinated cohort)

See template for **Table R 9**

Table R 16 Listing of SAEs

Group	Pid	Case Id	Age (Week)	Sex	Verbatim	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Causality	Outcome
HRV													

Age (week) = Age (week) at SAE onset

Table R 17 Number and percentage of doses and of subjects who took at least one concomitant medication from Day 0 to Day 7 after vaccination by type (Total vaccinated cohort)

	HRV				
				95% CI	
	N	n	%	LL	UL
Dose 1					
Any	Xxx	Xxx	Xxx	Xxx	Xxx
Any antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Prophylactic antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Any antibiotic	Xxx	Xxx	Xxx	Xxx	Xxx
Dose 2					
Any	Xxx	Xxx	Xxx	Xxx	Xxx
Any antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Prophylactic antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Any antibiotic	Xxx	Xxx	Xxx	Xxx	Xxx
Overall/dose					
Any	Xxx	Xxx	Xxx	Xxx	Xxx
Any antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Prophylactic antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Any antibiotic	Xxx	Xxx	Xxx	Xxx	Xxx
Overall/subject					
Any	Xxx	Xxx	Xxx	Xxx	Xxx
Any antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Prophylactic antipyretic	Xxx	Xxx	Xxx	Xxx	Xxx
Any antibiotic	Xxx	Xxx	Xxx	Xxx	Xxx

For each dose and overall/subject:

N= number of subjects with at least one administered dose

n/%= number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period

For overall/dose:

N= number of administered doses

n/%= number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period

95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table R 18 Number and percentage of doses and of subjects who took at least one concomitant medication during the entire study period by dose and overall (Total vaccinated cohort)

See template for Table R 17

Table KFDA 1 Summary of post marketing surveillance

Summary of post marketing surveillance			
General post marketing surveillance	Performance status (number of sites, number of subjects, etc) and future surveillance plan or reason for unexecution		
		Size of the population	Results
Surveillance on special patients	Surveillance on children (<18 years old)	212	Unsolicited symptoms were reported by 85 subjects within the 31-day post-vaccination period. Grade 3 unsolicited symptoms within the 31-day post-vaccination period was reported by 1 subject. Within the 7-day post-vaccination period, 34 subjects reported unsolicited symptoms.
	Surveillance on pregnant women	0	No relevant data/No relevant subjects.
	Surveillance on renal impairment patients	0	No relevant data/No relevant subjects.
	Surveillance on liver impairment patients	0	No relevant data/No relevant subjects.
	Surveillance on other special patients	0	No relevant data/No relevant subjects.

Table KFDA 2 Table of Subjects

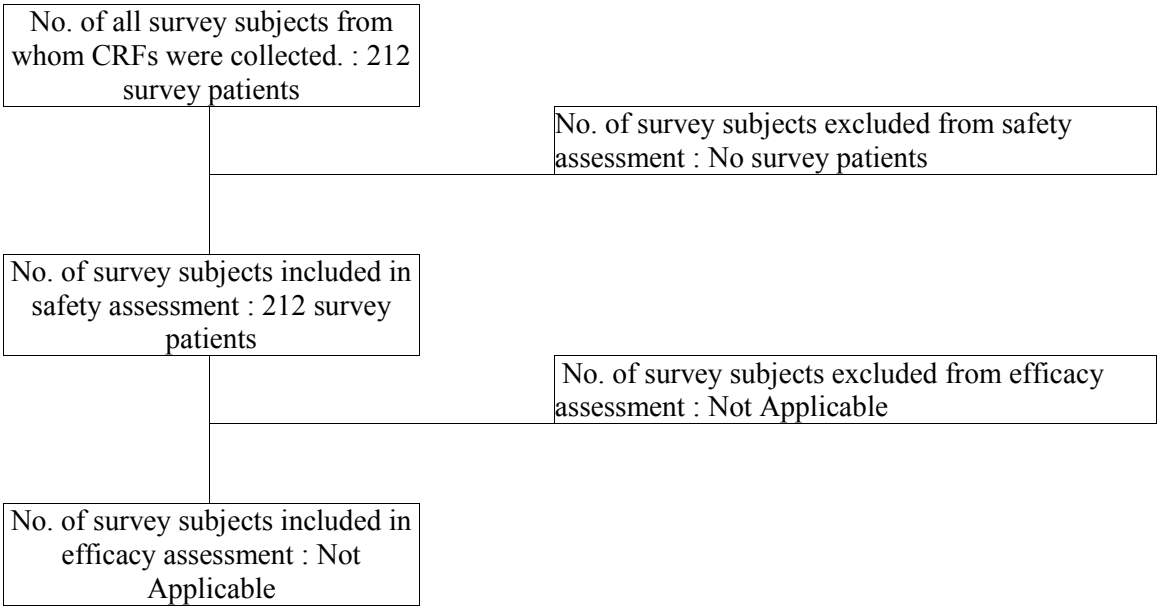

Table KFDA 3 Line-listing of AE

Incidence of adverse events (solicited and unsolicited) reported during the entire study period

Line-listing of AE								
Time / **Target**	**Before licence**	**Case report**						
		1st year	**2nd year**	**3rd year**	**4th year**	**5th year**	**6th year**	**Total**
Study institute (A) *No of sites*	-							
Subject included in the safety analysis Group(B)	-							
Subject with observed AE (C) No of subject who report ANY AEs	-							
Symptom reported as AE(D) No of reported AEs	-							
Incidence of AE(C/B)	-							

Adverse experience	**# of subjects who experienced Adverse events (solicited and unsolicited) (%), [#of events]**							
Period		**1st**	**2nd**	**3rd**	**4th**	**5th**	**6th**	**accumulated**
ENDOCRINE DISORDERS		**0 (0.0) [0]**			**3 (0.9) [3]**	**0 (0.0) [0]**	**0 (0.0) [0]**	**3 (0.3) [3]**
GROWTH HORMONE DEFICIENCY		0 (0.0) [0]			1 (0.3) [1]	0 (0.0) [0]	0 (0.0) [0]	1 (0.1) [1]
HYPOTHYROIDISM		0 (0.0) [0]			1 (0.3) [1]	0 (0.0) [0]	0 (0.0) [0]	1 (0.1) [1]

* Classification of symptom reported as AEs according to SOC.

Table KFDA 4 Line-Listing of Adverse Events with a causal relationship to vaccination.

Incidence of related symptoms (solicited and unsolicited) during the entire study period

Line-listing of AE								
Time / **Target**	**Before licence**	**Case report**						
		1st year	**2nd year**	**3rd year**	**4th year**	**5th year**	**6th year**	**Total**
Study institute (A)	-	8	-	-	22	9	8	47
Subject included in the safety analysis Group(B)	-	75	-	-	340	300	160	875
Subject observed AE (C)	-	4	-	-	14	78	59	155
Symptom reported as AE(D)	-	4	-	-	33	138	138	313
Incidence of AE(C/B)	-	5.3%	-	-	4.1%	26%	36.9%	17.7%

Adverse experience	**# of subjects who experienced Adverse events (solicited and unsolicited) (%), [#of events]**							
Period		**1st**	**2nd**	**3rd**	**4th**	**5th**	**6th**	**Accumulated**
ENDOCRINE DISORDERS		**0 (0.0) [0]**			**0 (0.0) [0]**	**0 (0.0) [0]**	**0 (0.0) [0]**	**0 (0.0) [0]**
GROWTH HORMONE DEFICIENCY		0 (0.0) [0]			0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
HYPOTHYROIDISM		0 (0.0) [0]			0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
PRECOCIOUS PUBERTY		0 (0.0) [0]			0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Table KFDA 5 Line-listing AEs from clinical trial and spontaneous report

Line-listing AEs from clinical trial and spontaneous report							
AEs	AEs						
	1st year	2nd year	3rd year	4th year	5th year	MR	comment
-	-	-	-	-	0		-

Table KFDA 6 Line-listing of reported SAE and unexpected ADR

This table should include all SAEs and unexpected (which is not listed on the local prescribing information) ADR.

Line-listing of reported SAE·and unexpected ADR							
SAE·ADR	**Reported cases (%)**						
	1st year	**2nd year**	**3rd year**	**4th year**	**5th year**	**MR**	**comment**
Kawasaki' disease	-	-	-	-	1		
Injection site pruritis	-	-	-	-	2		
Arthralgia	-	-	-	-	1		
Shipping amount							

Table KFDA 7 Contents of SAE and unexpected ADR

Details of KFDA specific Listings: Annex 6 (by each subject information)

Contents of SAE and unexpected ADR

No.	AE		gender	Age in weeks	Subject initial	ID or Patient No.	Date of onset	Severity	Causal relationship		Remark
	Body system organ	Specific terminology							Doctor	Company	
PPD	Systemic	Kawasaki's disease	M	67	-	PPD	30-10-2006	1	Y	-	Recovered
		Injection site pruritis	F	260	-	-	29-10-2006	1	Y	-	
	Knee	Arthralgia	F	284	-	-	02-11-2006	1	Y	-	
		Injection site pruritis	M	480	-	-	31-10-2006	2	Y	-	

Table KFDA 8 Line-listing of SAE and unexpected ADR

Detailed description of KFDA specific Listings: Annex 6 and 7 based on CRF contents

Serious adverse events, and unexpected adverse drug reaction summary table[1]													
Survey patients Name (initial)	Male? female	Age(year)	resident no. or chart no.	inpatient outpatient			pregnancy: no	history of AEs?ADRs no		major case history such as predisposition etc	number[5]		
PPD	male	2 years	PPD	name and site of hospital : PPD			occupation: None			yes	PPD		
product name (manufacturer)	generic name	S[2] ? O	Usage				reason for use underline the original disease and put complications in parenthesis	name of AEs?ADRs[3]	KAWASAKI Disease				
			route	daily dose	initiation	termination							
Fluarix™ (GSK biologicals)	Influenza vaccine	S	IM	0.25 mL	25/10/02006	25/10/02006	Flu prevention	dd/mmm/yyyy[4]	State or symptoms of adverse events and treatments against them etc		Whether the precautions for use were reflected or not etc.		
								PPD	Intensity: mild, Outcome: recovered/resolved This subject had fever, erythma and edema on palms, soles and BCG injection site. Both conjunctival infection and infected throat were examined. This subject was hospitalization from 03/NOV/2006 to 05/NOV/2006. Prescription was Sofenac inj, Miya-BM, Pseudoephedrein HCL, Polybutine Syr, Aspirin, Tylenol syr, Cernevit inj, Becomphexa 2mL/A, Furtman 10mL/V, Primene 10% 100mL, IV Globuline 500mg/10mL/B, Bepanthen 30mg, UNI-C 10g/20mL/V, Augmentin Duo Syr 7:1, SD inj (1:4) pack 500mg, Aminophyilline 100mg, Prospan syr. See details on individual data listing.		None applicable		
other treatment : no					readministration : no			results(dd/mmm/yyyy)			05/NOV/2006		

opinion of doctor in charge	Subject PPDhad fever on PPD visited hospital on 1/NOV/2006. Erythema and severe edema with pain observed on palms, soles and BCG injection site. Diagnosis was KAWASAKI disease and prescription was aspirin. (see details on individual data listing) But symptom didn't improve, so subject was hospitalization from 03/NOV/2006 to 05/NOV/2006. On 13/NOV/2006 deep desquamation was occurred on the tips of fingers and toes. Doctor evaluated causality with vaccine was unknown.	opinion of the reporting organization	This SAE occurred day 5 after vaccination. And It was difficult to say there is no relationship obviously. Therefore company evaluated causality was yes.	treatment and future plan	Occurrence of this SAE will be observed through spontaneous report and PSUR.

Table KFDA 9 Individual Line-listing for All Subjects

1)

Line-listing of subjects (background of subjects)

Subject No.	Name of center	Resident Registration Number	Gender	Age (months)	Weight (Kg)	Height (Cm)
PPD			Female	31	6.4	60
			male	17	6.1	61
			male	8	6.5	62
			male	8	5.1	56

2)

Line-listing of subjects (medical history)

Subject No.	Name of center	Diagnosis	Past/ Current
PPD		pneumonia	past
			current
			current

3)

Line-listing of subjects (vaccine administration)

Subject No.	Name of center	Indication	Dose	Date of vaccine administration	Route	Site		Administrated according to protocol?
PPD		Prevent Varicella	3	17-Jul-07	IM	thigh	Left	Yes

4)

Line-listing of subjects (solicited adverse events)

Subject	Name	AE	Dose	Intensity

No.	of center			Day0	Day1	Day2	Day3	Day4	Day5	Day6
PPD		drowsiness	2	0	1	0	0	0	0	0
		irritation	1	0	1	0	0	0	0	0
		loss of appetite	1	1	1	1	1	1	0	0

5)

Line-listing of subjects (unsolicited adverse events)

Subject No.	Name of center	AE	Causality/Relationship to investigational products According to KFDA standards	Start date	End date	Outcome
PPD		Dermatitis	Probably not related	30-Jul-07	31-Jul-07	recovered

6)

Line-listing of subjects (concomitant medication)

Subject No.	Name of center	Dose	Trade/Generic name	Medical indication	Total daily dose	Route	Start date	End date	medication is Ongoing? (Yes/No)
PPD		1							
		1							
		1							

7)

Line-listing of subjects (concomitant vaccination)

Subject No.	Name of center	Trade/Generic name	Administration date	Route

Table CTRS 1 Demography for CTRS

Number of subjects	**HRV**
Planned, N	
N (Total Vaccinated Cohort)	
Completed, n (%)	
Total Number Subjects Withdrawn, n (%)	
Withdrawn due to Adverse Events, n (%)	
Withdrawn for other reasons, n (%)	
Demographics	**HRV**
N (Total Vaccinated Cohort)	
Females:Males	
Mean Age, weeks (SD)	
White/caucasian, n (%)	

Table CTRS 2 Number (%) of subjects with solicited general symptom during the 8-day (Days 0-7) post-vaccination period (Total Vaccinated Cohort)

		HRV				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1						
Cough /Runny nose	All					
	Grade 3					
	Related					
Diarrhoea	All					
	Grade 3					
	Related					
Fever/(Axillary) (°C)	All					
	Grade 3					
	Related					
Irritability	All					
	Grade 3					
	Related					
Loss of appetite	All					
	Grade 3					
	Related					
Vomiting	All					
	Grade 3					
	Related					
Dose 2						
Cough /Runny nose	All					
	Grade 3					
	Related					
Diarrhoea	All					
	Grade 3					
	Related					
Fever/(Axillary) (°C)	All					
	Grade 3					
	Related					
Irritability	All					
	Grade 3					
	Related					
Loss of appetite	All					
	Grade 3					
	Related					
Vomiting	All					
	Grade 3					
	Related					
Across doses						
Cough /Runny nose	All					
	Grade 3					

		HRV				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
	Related					
Diarrhoea	All					
	Grade 3					
	Related					
Fever/(Axillary) (°C)	All					
	Grade 3					
	Related					
Irritability	All					
	Grade 3					
	Related					
Loss of appetite	All					
	Grade 3					
	Related					
Vomiting	All					
	Grade 3					
	Related					

N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting a specified symptom
95%CI, LL and UL = Exact 95% confidence interval, lower and upper limit
Any = all reports of the specified symptom irrespective of intensity grade and relationship to vaccination

Table CTRS 3 Number (%) of subjects with adverse events (Total vaccinated cohort)

Most frequent adverse events - On-Therapy (occuring within day 0-30 following vaccination)	**HRV N = XXX**
Subjects with any AE(s), n(%)	
Rhinitis	
Nervousness	
Fever	
upper resp tract infection	
Conjunctivitis	
Coughing	
otitis media	
Gastroesophageal reflux	
Flatulence	
Fatigue	
abdominal pain	
crying abnormal	
tooth ache	4 (2.3)

Table CTRS 4 Number (%) of subjects with serious adverse events (Total vaccinated cohort)

All SAEs	**HRV N = XXX**
Subjects with any SAE(s), n(%) [n related]	
Appetite increased	
Asthma	
Bronchitis	
Crying abnormal	
Eczema	
Fever	
Gastroenteritis	
infection bacterial	
infection viral	
Injury	
Laryngitis	
Meningitis	
otitis media	
Pneumonia	
Seborrhea	
Somnolence	
upper resp tract infection	
All fatal SAEs	**HRV N = XXX**
Subjects with any SAE(s), n(%) [n related]	

Table KFDA 10 Demographic data - by gender/race

		Male N=	Female N=	Total N=
Age (Weeks)	Mean			
	Range			
	SD			

		Male N=	Female N=	Total N=
Race	Korean			
	Non-Korean			

Table KFDA 11 Pre-exist medical history – by gender

		Male N =		Female N =		Total N =	
		n	%	n	%	n	%
Medical History	Yes						
	No						
	Total						
BLOOD AND LYMPHATIC SYSTEM	Yes						
	No						
	Total						
CARDIAC	Yes						
	No						
	Total						

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified category(Yes/No)

Table KFDA 12 pre-exist medical history - by classification

Past Medical History	Diagnosis or Sign Symptom	N	n	%	95% CI LL	95% CI UL
BLOOD AND LYMPHATIC SYSTEM	ANEMIA					
	NEUTROPENIA					
	SEPSIS					
	SEPSIS NEWBORN					
CARDIAC	ASD. TR.					
	ATRIAL SEPTAL DEFECT					
	PUL. HTN					
	TRICUSPID REGURGITATION					

N= Number of subjects with the specified medical history
n(%) = number(percentage) of subjects with the specified category of diagnosis or symptom
95%CI = 95% confidence interval; LL, UL = lower and upper confidence limits

Table KFDA 13 Pre-rotavirus vaccination history

		Male N=		Female N=		Total N=	
		n	%	n	%	n	%
Rotavirus vaccination	Yes						
	No						

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified category(Yes/No)

Table KFDA 14 Administration of concomitant medication – by gender

		Male N=		Female N=		Total N=	
		n	%	n	%	n	%
Administration of concomitant medication	Yes						
	No						
	Total						

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified category(Yes/No)

Table KFDA 15 Administration of concomitant medication – by classification

Classification	N	n	%	95% CI	
				LL	UL
Any					
Any antipyretic					
Prophylactic antipyretic					
Any antibiotic					

N= Number of subjects
n(%) = number(percentage) of subjects with the specified classification
95%CI = 95% confidence interval; LL, UL = lower and upper confidence limits

Table KFDA 16 Administration of concomitant vaccination

		N	
		n	%
Administration of concomitant vaccination	Yes		
	No		
	Total		

N= Number of subjects)
n(%) = number(percentage) of subjects with the specified category(Yes/No)

Table KFDA 17 Administration of study vaccination – by gender

		Male N=		Female N=		Total N=	
		n	%	n	%	n	%
Administration of study vaccination	Dose1						
	Dose 2						
	Total						

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified category(Yes/No)

Table KFDA 18 Summary of serious adverse events, adverse drug reactions

Primary System Organ Class (Code)	Preferred Term (Code	SAE						Serious ADR					
						95% CI						95% CI	
		N	n	n*	%	LL	UL	N	n	n*	%	LL	UL

N= Number of subjects
n(%) = number(percentage) of subjects with the specified category; 95%CI = 95% confidence interval; LL, UL = lower and upper confidence limits
n* = number of symptoms of the specified category

Table KFDA 19 Serious adverse events, adverse drug reactions

Event	Start date	End date	Severity	Causality	Outcome	Change on medication

Table KFDA 20 Adverse events, adverse drug reactions

Expected (**solicited**) adverse events and adverse drug reactions

Events	AE						ADR					
					95% CI						95% CI	
	N	n	n*	%	LL	UL	N	n	n*	%	LL	UL
Fever												
Fussiness/irritabiliy												
Diarrhoea												
vomitting												
Loss of appetite												
Cough/Runny nose												

N= Number of subjects
n(%) = number(percentage) of subjects with the specified category; 95%CI = 95% confidence interval; LL, UL = lower and upper confidence limits
n* = number of symptoms of the specified category

Unexpected (**unsolicited**) adverse events and adverse drug reactions

Primary System Organ Class (Code)	Preferred Term (Code	AE						ADR					
						95% CI						95% CI	
		N	n	n*	%	LL	UL	N	n	n*	%	LL	UL

N= Number of subjects
n(%) = number(percentage) of subjects with the specified category; 95%CI = 95% confidence interval; LL, UL = lower and upper confidence limits
n* = number of symptoms of the specified category

Table KFDA 21 Adverse events (Solicited and Unsolicited) experienced by subjects during the entire study period; stratified by gender (Total vaccinated cohort)

Factor	Category	N	Subject experienced any adverse event (solicited or unsolicited)							
			Yes				No			
					95 % CI				95 % CI	
			n	%	LL	UL	N	%	LL	UL
Gender	Male									
	Female									

N=Number of subjects in the given category
n/%= number/percentage of subjects in the given category

Table KFDA 22 Adverse events (Solicited and Unsolicited) experienced by subjects during the entire study period; stratified by age (Total vaccinated cohort)

See template for Table KFDA 12

Table KFDA 23 Adverse events (Solicited and Unsolicited) experienced by subjects at any time during the study; stratified by concomitant medication (Total vaccinated cohort)

See template for Table KFDA 12

Table KFDA 24 Adverse events (Solicited and Unsolicited) experienced by subjects at any time during the study; stratified by concomitant vaccination (Total vaccinated cohort)

See template for Table KFDA 12

Table KFDA 25 Adverse events experienced by subjects at any time during the study; stratified by past medical history status (Total vaccinated cohort)

See template for Table KFDA 12

Table KFDA 26 Adverse events by medical history – by gender & classification

Past Medical History	Adverse events	Male N=		Female N=		Total N=	
		n	%	n	%	n	%
BLOOD AND LYMPHATIC SYSTEM							
CARDIAC							

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified category(Adverse events)

Table KFDA 27 Adverse events by concomitant medication – by classification

Classification	N	Adverse events					
		Yes		No		Total	
		n	%	n	%	n	%
Any							
Any antipyretic							
Prophylactic antipyretic							
Any antibiotic							

N= Number of subjects
n(%) = number(percentage) of subjects with the specified Classification

Table KFDA 28 Adverse events by concomitant vaccinations – by Classification

Classification	Male N=		Female N=		Total N=	
	n	%	n	%	n	%
Any						
BCG						
DTPA						

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified Classification

Table KFDA 29 Adverse events by medical history, Concomitant vaccination, concomitant medication

		Medical History				Concomitant Medication				Concomitant vaccination			
		Yes		No		Yes		No		Yes		No	
	N	n	%	n	%	n	%	n	%	n	%	n	%
Expected (Solicited) Adverse events													
Fever													
Loss of appetite													
Total (Expected adverse events)													
Unexpected (unsolicited) Adverse events													
Total (Unexpected adverse events)													

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified Classification

Table KFDA 30 Adverse events by duration

		Day 0		Days 1		Days 2		Days 3		Days 4-7		Days 8-15		Days 16-30		Days >30	
	N	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Expected (solicited) adverse events																	
Total																	
Unexpected(unsolicited) adverse events																	
Total																	

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified Classification

Table KFDA 31 Adverse events by severity

	N	Mild		Moderate		Severe	
		n	%	n	%	n	%
Dose1							
Expected (Solicited) adverse events							
Total							
Unexpected (Unsolicited) adverse events							
Total							
Dose 2							
Expected (Solicited) adverse events							
Total							
Unexpected (Unsolicited) adverse events							
Total							

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified Classification

Table KFDA 32 Adverse events by causality

	N	Certain		Probable/Likely		Possible		Unlikely		Conditional/Unclassified	
		n	%	n	%	n	%	n	%	n	%
Dose1											
Expected (Solicited) adverse events											
Total											
Unexpected (Unsolicited) adverse events											
Total											
Dose 2											
Expected (Solicited) adverse events											
Total											
Unexpected (Unsolicited) adverse events											
Total											

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified Classification

Table KFDA 33 Adverse events by outcome

	N	Recovered/Resolved		Not recovered/Not resolved		Recovering/resolving		Recovered with sequelae/resolved with sequelae		unknown	
		n	%	n	%	n	%	n	%	n	%
Dose1											
Expected (Solicited) adverse events											
Total											
Unexpected (Unsolicited) adverse events											
Total											
Dose 2											
Expected (Solicited) adverse events											
Total											
Unexpected (Unsolicited) adverse events											
Total											

N= Number of subjects in each group(Male/Female)
n(%) = number(percentage) of subjects with the specified Classification

6. ANNEX 2: CRITERIA FOR ELIMINATING SUBJECTS FROM STAT ANALYSES

Provided as a separate document

Statistical Analysis Plan Approval

Protocol Title:	Open, multi-centric, post-marketing surveillance (PMS) to monitor the safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe) when administered according to the prescribing information in Korea.
eTrack study number	111700
eTrack abbreviated title	(Rota-070 PMS)
Protocol version/date	Amendment 4: 23 February 2012
Scope:	All data pertaining to the above study
Version:	Amendment 2
Date:	18-Dec-2013
Co-ordinating author:	PPD
Other author(s):	

Approved by:

Lead Clinical Development, Combination Vaccines and Rotavirus Vaccines	PPD		
	Name	Signature	dd-mmm-yyyy
Project Statistician	PPD		
	Name	Signature	dd-mmm-yyyy
Lead Statistician	PPD		
	Name	Signature	dd-mmm-yyyy

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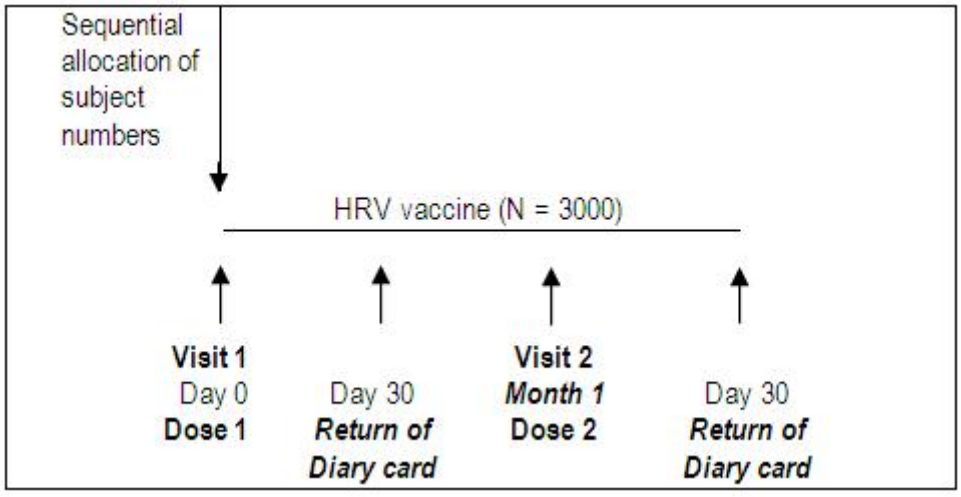
1. DOCUMENT HISTORY

Date	Version	Description
12-Dec-2011	First Version	First approved version
15-Feb-2013	Amendment 1	• Amendment of the SAP is done to consistent with the Protocol Amendment 4: 23 February 2012 • Planned analysis Changed in the section 6.1.2 and Section 9 as All the planned analysis will be performed on the basis of WHOART and not based on MedDRA.
18-Dec-2013	Amendment 2	• Planned analysis Changed in the section 6.1.2

2. STUDY DESIGN



N: Number of subjects planned to be enrolled.
Infants who have received a dose of the vaccine prior to the start of the PMS will have only one visit followed by the phone contact.
PMS conclusion: An infant's parent/guardian who will be contacted to provide details of any AEs experienced by the infant 30 days after the infant receives the last vaccination or an infant for whom diary card transcription into CRF will be been done through phone contact is considered to have completed the PMS.

- PMS design: Open-label, non-comparative, multi-centre PMS in Korea.
- Vaccination schedule: Two doses of Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe) will be administered orally as per the prescribing information in Korea.
  - First vaccination will be given to infants from the age of 6 weeks.
  - Second vaccination will be given at least 4 weeks after Dose 1. Administration of Dose 2 is preferably given before the age of 16 weeks.

Two doses of Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe) should be given before 24 weeks of age.

- Control: None.
- Type of PMS: Self-contained.
- Two visits are recommended as follows:
  - Visit 1: Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe) vaccination, subjects will be allowed to receive concomitant vaccinations.
  - Visit 2: Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe) vaccination, subjects will be allowed to receive concomitant vaccinations.
- Recording of AEs from Day 0 to Day 30 using diary cards after each dose of Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe).
- Recording of SAEs during the entire PMS period.
- Duration of the PMS: The intended duration of the PMS, per infant, will be approximately 3 months.
- Refer to Appendix B for details of the recruitment plan.
- Data collection: Standardised hard copy case report form (CRF).

3. OBJECTIVES

To assess the safety of Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe) in infants when administered according to the prescribing information in Korea.

Refer to Section 4 for definition of the endpoints.

4. ENDPOINTS

- Occurrence of AEs during the 31-day (Day 0 – Day 30) follow-up period after each vaccine dose according to Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of SAEs during the entire PMS period.

5. STUDY POPULATION

5.1.1. Total Vaccinated cohort

The total vaccinated cohort will include all vaccinated subjects with at least one dose of Rotarix™ or Rotarix™ liquid formulation (oral suspension or prefilled syringe) administration documented:

- A safety analysis based on the total vaccinated cohort will include all vaccinated subjects.

Cohort	Elimination codes	Eli Type
Total vaccinated cohort	1030	MA

6. STATISTICAL METHODS

Statistical analyses will be performed as per the requirements ***for the*** KFDA ***submission.***

6.1.1. Analysis of demographics/baseline characteristics

The mean, range and standard deviation of age in weeks at each dose will be calculated. The racial, rotavirus vaccination history and gender composition of the vaccinated subjects will be also presented.

The distribution of subjects enrolled among the PMS centres will be tabulated.

6.1.2. Analysis of safety

The verbatim reports of AEs will be reviewed by a physician and the signs and symptoms will be coded according to WHOART. Every verbatim term will be matched with the appropriate Preferred Term. As per regulatory requirement, all the planned analysis ***of***

AE after the SAP Amendment 1 dated 15 February 2013 will be performed on the basis of WHOART and not based on MedDRA.

The analysis of safety will be performed according to expectedness (see Abbreviations). Expectedness will be derived from the ***WHOART*** PT classification. The list of primary PT associated to expected adverse events will be reviewed before each database freeze for analysis.

The number and percentage of subjects with AEs occurring within 31 days with its exact 95% CI will be tabulated by preferred term. Similar tabulations will be done for the number and percentage of subjects with SAEs during the study period.

Number and percentage of expected adverse events and adverse drug reactions along with the exact 95% CI will be tabulated. Number and percentage of expected AEs and ADRs by SOC and PT will be tabulated.

Number and percentage of unexpected adverse events and adverse drug reactions along with the exact 95% CI will be tabulated. Number and percentage of unexpected AEs and ADRs by SOC and PT will be tabulated.

Serious adverse events reported during the study period will also be summarized.

The percentage of subjects who received at least one concomitant medication/vaccination will be tabulated by type of medication, with exact 95% CI. Similar tabulations will be done for subjects who receive concomitant medication/vaccination during the entire PMS period.

Summary of Adverse events by duration, severity, causality and outcome will be performed to reflect the KFDA requirements.

In addition, specific statistical analyses (e.g. AEs classified by gender, past medical history, concomitant medication/vaccination etc) will be performed to reflect the KFDA requirements

7. STATISTICAL CALCULATIONS

7.1. Derived and transformed data

Infants who missed reporting symptoms (AEs or concomitant medications) will be treated as infants without symptoms (AEs or concomitant medications, respectively). In case of significant non-compliance of PMS procedures for reporting symptoms, the analysis plan will be reassessed to ensure more accurate reporting of PMS data by further analysis.

7.2. Data presentation description

The following decimal description will be used for the demography, reactogenicity/Safety.

Display Table	Parameters	Number of decimal digits
All summaries	% of count, including LL & UL of CI	1
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	2

7.3. Group description

The following group will be used for the statistical analyses.

Study	Group order in tables	Group label in tables
Rota_070	1	HRV

7.4. Methodology for computing CI

All CI will be 2 sided 95% CI.

- The exact 95% CIs for proportion within a group will be based on the method by Clopper

Refer to Section 10 for references.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

Description	Analysis ID (SDD sub-folder)	TFL short title
Analysis year 3 & year 4	ANALYSIS_E1_01	For year 3,4,5
Analysis year 5	ANALYSIS_E1_03	For year 3,4,5
Analysis year 6	ANALYSIS_E1_04	Comprehensive report

8.2. Statistical considerations for interim analyses

Annual reports will be written for 6 years. The last annual report will be replaced by a comprehensive report. All analyses described above will be performed on cleaned data for each annual report. The analysis, including individual data listings, will be cumulative and based on the cohort for vaccinated subjects for which the PMS conclusion page has been received at GSK before the pre-defined cut-off date. All reports will be sent to the GSK Biologicals' Central Safety and Pharmacovigilance (BCSP).

9. CHANGES FROM PLANNED ANALYSES

- The verbatim reports of AEs will be reviewed by a physician and the signs and symptoms will be coded according to WHOART. Every verbatim term will be matched with the appropriate Preferred Term. As per regulatory requirement, all the planned analysis after the SAP Amendment 1 dated 15 February 2013 will be performed on the basis of WHOART and not based on MedDRA.

- ***Number and percentage of expected adverse events and adverse drug reactions along with the exact 95% CI will be tabulated. Number and percentage of expected AEs and ADRs by SOC and PT will be tabulated.***
- ***Number and percentage of unexpected adverse events and adverse drug reactions along with the exact 95% CI will be tabulated. Number and percentage of unexpected AEs and ADRs by SOC and PT will be tabulated.***
- ***Summary of Adverse events by duration, severity, causality and outcome will be performed.***

10. REFERENCES

- Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. Biometrika. 1934;26:404-413.

11. ABBREVIATIONS

AE	Adverse event
CI	Confidence Interval
CRF	Case Report Form
GSK	GlaxoSmithKline
MedDRA	Medical Dictionary for Regulatory Activities
SAE	Serious Adverse Event
HRV	Human rotavirus
LL	Lower limit
UL	Upper limit
SD	Standard deviation
PMS	Post Marketing Surveillance
RV	Rotavirus
KFDA	Korean Food and Drugs Administration
WHOART	WHO Adverse Reaction Terminology
Expected adverse event	The presence/occurrence/intensity of an adverse event that is expected from the infant or an observer during the post-vaccination follow-up period as described in the locally approved prescribing information
Unexpected adverse event	Any adverse event that is not reflected in the locally approved prescribing information

GlaxoSmithKline	Rota-070 (111700)	Center No. : |_|_|_|_|_|	Subject No.: |_|_|_|_|_|_|	Date of Visit1: |_|_| |_|_|_| |_|_|_|_| DD MMM YYYY

ROTARIX (Rota-070) PMS CRF

INFORMED CONSENT

I certify that Informed Consent has been obtained prior to any study procedure |_|_| |_|_|_| |_|_|_|_| DD MMM YYYY

DEMOGRAPHICS

Date of Birth: |_|_| |_|_|_| |_|_|_|_| DD MMM YYYY

Race: [1] ☐Korean (*) Codelist RACE_108344 [99] ☐Non-Korean, specify: _____ For GSK

Gender: [M] ☐ Male [F] ☐ Female

ELIGIBILITY CHECK

-Do not enter the subject into the study if he/she failed any inclusion or exclusion criteria below

Did the subject meet all the entry criteria?: ☐Yes ☐ No→ If No, tick (√) all boxes corresponding to violation of any inclusion/exclusion criteria.

INCLUSION CRITERIA

[1] ☐ Infants who the investigator believes that their parents/guardians can and will comply with the requirements of the protocol (e.g. completion of the diary cards) should be enrolled in the PMS.

[2] ☐ A male or female aged 6 weeks and above at the time of the first vaccination. (Note: Two doses of the Rotarix™ vaccine should be completed by the age of 24 weeks).

[3] ☐ Written informed consent obtained from the parent or guardian of the infant.

EXCLUSION CRITERIA

[4] ☐ At the time of PMS entry, the contraindications and precautions of use indicated in the prescribing information should be checked and the infant must not be included in the PMS if there is any contraindication. Any changes in the locally approved Prescribing Information must be implemented immediately.

GENERAL MEDICAL HISTORY / PHYSICAL EXAMINATION

Are you aware of any pre-existing conditions, signs or symptoms present prior to the start of the study?
☐ No ☐ Yes → Please give diagnosis and tick (√) appropriate Past/Current box(es)

MedDRA System Organ Class	Diagnosis	Past/Current	MedDRA System Organ Class	Diagnosis	Past / Current
[1] Skin and subcutaneous tissue		☐ ☐	[10] Eye		☐ ☐
		☐ ☐			☐ ☐
For GSK			For GSK		
[2] Musculoskeletal and connective tissue		☐ ☐			☐ ☐
		☐ ☐	[11] Ear and labyrinth		☐ ☐
For GSK			For GSK		
[3] Cardiac		☐ ☐	[12] Endocrine		☐ ☐
		☐ ☐			☐ ☐
For GSK			For GSK		
[4] Vascular		☐ ☐	[13] Metabolism and nutrition		☐ ☐
		☐ ☐			☐ ☐
For GSK			For GSK		
[5] Respiratory, thoracic and mediastinal		☐ ☐	[14] Blood and lymphatic system		☐ ☐
		☐ ☐			☐ ☐
For GSK			For GSK		
[6] Gastrointestinal		☐ ☐	[15] Immune system (Incl allergies, autoimmune disorders)		☐ ☐
		☐ ☐			☐ ☐
For GSK			For GSK		
[7] Hepatobiliary		☐ ☐	[16] Infections and infestations		☐ ☐
		☐ ☐			☐ ☐
For GSK			For GSK		
[8] Renal and urinary		☐ ☐	[17] Neoplasms benign, malignant and unspecified (including cysts and polyps)		☐ ☐
		☐ ☐			☐ ☐
For GSK			For GSK		
[9] Nervous system		☐ ☐	[18] Surgical and medical procedures		☐ ☐
		☐ ☐			☐ ☐
			[99] Other		☐ ☐
For GSK			For GSK		

PREVIOUS ROTAVIRUS VACCINATION HISTORY

Has the subject received any vaccination previously to Rotavirus? ☐No ☐Unknown ☐Yes→If Yes, please complete the table below

Trade/Generic Name		Dose No.	Est. Date of vaccination (DD MMM YYYY)
	For GSK		
	For GSK		
	For GSK		

GlaxoSmithKline	Rota-070 (111700)	Center No : _____	Subject No : _____	Visit 1

VACCINE ADMINISTRATION
Date if different from visit date: __/__/____ (DD MMM YYYY)
Pre-vaccination temperature : __._ °C
Tick the most appropriate box(es) → [A] ☐ Axillary [O] ☐ Oral [T] ☐ Tympanic

Vaccine Administration Please tick (√) the most appropriate box(es) ← VACCPROD. DOSE	Route	Has the study vaccine been administered according to the protocol?
☐ Rotarix™ ☐ 1st Dose ☐ 2nd Dose	Oral	☐ Yes
☐ Not administered-->Please complete below (*)		☐ No → Please comment: _____

(*) Why not administered? Please tick (√) the major reason for non administration
- ☐ [SAE] Serious adverse event → Please complete the Serious Adverse Event form and specify SAE No. ____
- ☐ [AEX] Non-Serious adverse event →Complete the Non-serious Adverse Event section and specify AE No. ____
- ☐ [OTH] Other, please specify (e.g.: consent withdrawal, protocol violation…): _____ /For GSK _____
- → Please tick who made the decision? [I] ☐ Investigator [P] ☐ Parents/Guardians

SOLICITED ADVERSE EVENTS- GENERAL SYMPTOMS*

Has the subject experienced any of the following signs/symptoms during the solicited period?
[N] ☐ No [Y] ☐ Yes, Please tick (√) No/Yes for each symptom. If Yes is ticked, complete all items [U] ☐ Information not available [NA] ☐ No vaccine administered

GENERAL SYMPTOMS	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Ong oing after day 7?	Date of last day of symptoms (DDMMM YYYY)	Causality / Relationship to investigational products According to KFDA	Medically attended visit?	
Temperature (FE) ☐ No ☐ Yes→ °C ☐ Axillary ☐ Oral ☐ Tympanic	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ No ☐ Yes →	__/__/____ ____	[1] ☐ Definitely related [2] ☐ Probably related [3] ☐ Possibly related [4] ☐ Probably not related [5] ☐ Unknown	☐ No ☐ Yes →	___ HO/ER/MD
Irritability/Fussiness (IR) ☐ No ☐ Yes → Intensity									☐ No ☐ Yes →	__/__/____ ____	[1] ☐ Definitely related [2] ☐ Probably related [3] ☐ Possibly related [4] ☐ Probably not related [5] ☐ Unknown	☐ No ☐ Yes →	___ HO/ER/MD
Diarrhoea (DA) ☐ No ☐ Yes → number of loose stools									☐ No ☐ Yes →	__/__/____ ____	[1] ☐ Definitely related [2] ☐ Probably related [3] ☐ Possibly related [4] ☐ Probably not related [5] ☐ Unknown	☐ No ☐ Yes →	___ HO/ER/MD
Vomiting (VO) ☐ No ☐ Yes → number of vomits									☐ No ☐ Yes →	__/__/____ ____	[1] ☐ Definitely related [2] ☐ Probably related [3] ☐ Possibly related [4] ☐ Probably not related [5] ☐ Unknown	☐ No ☐ Yes →	___ HO/ER/MD
Loss of appetite (LO) ☐ No ☐ Yes → Intensity									☐ No ☐ Yes →	__/__/____ ____	[1] ☐ Definitely related [2] ☐ Probably related [3] ☐ Possibly related [4] ☐ Probably not related [5] ☐ Unknown	☐ No ☐ Yes →	___ HO/ER/MD
Cough/runny nose (CO) ☐ No ☐ Yes → Intensity									☐ No ☐ Yes →	__/__/____ ____	[1] ☐ Definitely related [2] ☐ Probably related [3] ☐ Possibly related [4] ☐ Probably not related [5] ☐ Unknown	☐ No ☐ Yes →	___ HO/ER/MD

* If any of these adverse events meets the protocol definition of serious, please complete and submit a Serious Adverse Event report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

Intensity: 0/1/2/3 See AE definition

Fever: Axillary, Oral & Tympanic ≥ 37.5°C

Medically Attended Visit →

HO : Hospitalization
ER : Emergency Room
MD: Medical Personnel

UNSOLICITED ADVERSE EVENT

Has the subject experienced any serious or non-serious unsolicited adverse events within 31 days of follow up of post-vaccination?
[N] ☐ No [Y] ☐ Yes, fill in the Non-Serious Adverse Event section or SAE Report as necessary* [U] ☐ Information not available [NA] ☐ No vaccine administered

TELEPHONE CONTACT
Day 8-30 after vaccination __/__/____ (DD MMM YYYY)

Has safety information been obtained ?
- ☐ No, please complete above the date attempt of last phone contact.
- ☐ Yes, please complete the date of telephone contact above.

GlaxoSmithKline	Rota-070 (111700)	Center No. :	Subject No.:	Date of Visit 2: DD MMM YYYY

CHECK FOR STUDY CONTINUATION if subject received 2nd dose on visit1, skip to the study conclusion pg.

Did the subject come for the 2nd visit? ☐Yes ☐No→Please tick (√) the one most appropriate reason skip the following pages of this visit

☐ [SAE] Serious adverse event → Please complete the Serious Adverse Event form and specify SAE No. ☐☐
☐ [AEX] Non-Serious adverse event →Complete the Non-serious Adverse Event section and specify AE No. ☐☐ or solicited AE code ☐☐
☐ [OTH] Other, please specify (e.g.: consent withdrawal, protocol violation…): _____ / For GSK _____
→ Please tick who made the decision? [I] ☐ Investigator [P] ☐Parents/Guardians

VACCINE ADMINISTRATION Date if different from visit date ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Pre-vaccination temperature : ☐☐.☐ °C
Tick the most appropriate box(es) → [A] ☐Axillary [O] ☐Oral [T] ☐Tympanic

Vaccine Administration Please tick (√) the most appropriate box(es)	Route	Has the study vaccine been administered according to the protocol?
☐Rotarix™ ☐2nd Dose	Oral	☐Yes
☐Not administered-->Please complete below (*)		☐No → Please comment: _____

(*) Why not administered? Please tick (√) the major reason for non administration

☐ [SAE] Serious adverse event → Please complete the Serious Adverse Event form and specify No. ☐☐
☐ [AEX] Non-Serious adverse event →Complete the Non-serious Adverse Event section and specify AE No. ☐☐ or solicited AE code ☐☐
☐ [OTH] Other, please specify (e.g.: consent withdrawal, protocol violation…): _____ / For GSK _____
→ Please tick who made the decision? [I] ☐ Investigator [P] ☐Parents/Guardians

SOLICITED ADVERSE EVENTS- GENERAL SYMPTOMS*

Has the subject experienced any of the following signs/symptoms during the solicited period?
[N]☐No [Y]☐Yes, Please tick (√) No/Yes for each symptom. If Yes is ticked, complete all items [U]☐ Information not available [NA]☐No vaccine administered

GENERAL SYMPTOMS	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Ongoing after day 7?	Date of last day of symptoms (DDMMM YYYY)	Causality / Relationship to investigational products According to KFDA	Medically attended visit?	
Temperature (FE) ☐No ☐Yes→°C ☐Axillary ☐Oral ☐Tympanic	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐ not taken	☐No ☐Yes →	☐☐ ☐☐☐ ☐☐☐☐	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐Unknown	☐No ☐Yes→	☐☐☐ HO/ER/MD
Irritability/Fussiness (IR) ☐No ☐Yes → Intensity									☐No ☐Yes →	☐☐ ☐☐☐ ☐☐☐☐	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐Unknown	☐No ☐Yes→	☐☐☐ HO/ER/MD
Diarrhoea (DA) ☐No ☐Yes → number of loose stools									☐No ☐Yes →	☐☐ ☐☐☐ ☐☐☐☐	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐Unknown	☐No ☐Yes→	☐☐☐ HO/ER/MD
Vomiting (VO) ☐No ☐Yes → number of vomits									☐No ☐Yes →	☐☐ ☐☐☐ ☐☐☐☐	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐Unknown	☐No ☐Yes→	☐☐☐ HO/ER/MD
Loss of appetite (LO) ☐No ☐Yes → Intensity									☐No ☐Yes →	☐☐ ☐☐☐ ☐☐☐☐	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐Unknown	☐No ☐Yes→	☐☐☐ HO/ER/MD
Cough/runny nose (CO) ☐No ☐Yes → Intensity									☐No ☐Yes →	☐☐ ☐☐☐ ☐☐☐☐	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐Unknown	☐No ☐Yes→	☐☐☐ HO/ER/MD

* If any of these adverse events meets the protocol definition of serious, please complete and submit a Serious Adverse Event report to GSK Biologicals Study Contact for SAE reporting within 24 hours.

Intensity: 0/1/2/3 See AE definition

Fever: Axillary, Oral & Tympanic ≥ 37.5°C

Medically Attended Visit →

HO : Hospitalization
ER : Emergency Room
MD: Medical Personnel

UNSOLICITED ADVERSE EVENT

Has the subject experienced any serious or non-serious unsolicited adverse events within 31 days of follow up of post-vaccination?
[N]☐No [Y]☐Yes, fill in the Non-Serious Adverse Event section or SAE Report as necessary* [U]☐ Information not available [NA]☐ No vaccine administered

TELEPHONE CONTACT

Day 8-30 after vaccination ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Has safety information been obtained?
☐ No, please complete above the date attempt of last phone contact.
☐ Yes, please complete the date of contact above.

GSK GlaxoSmithKline	Rota-070 (111700)	Center No.: |_|_|_|_|_|_|	Subject No.: |_|_|_|_|_|_|	Non serious adverse event 1

NON SERIOUS ADVERSE EVENT (Please report all serious adverse events only on Serious Adverse Event (SAE) Reports)

Has any non-serious adverse events occurred within one month (minimum 30 days) post-vaccination, excluding those recorded on the Solicited Adverse Events pages?

☐ No ☐ Yes → please complete the following table.

AE no.	1	2	3	4	5
Description	________	________	________	________	________
For GSK					
Date Started	|_|_||_|_|_||_|_|_|_| DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	|_|_||_|_|_||_|_|_|_| DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	|_|_||_|_|_||_|_|_|_| DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	|_|_||_|_|_||_|_|_|_| DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	|_|_||_|_|_||_|_|_|_| DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)
Date Stopped	|_|_||_|_|_||_|_|_|_| DD MMM YYYY	|_|_||_|_|_||_|_|_|_| DD MMM YYYY	|_|_||_|_|_||_|_|_|_| DD MMM YYYY	|_|_||_|_|_||_|_|_|_| DD MMM YYYY	|_|_||_|_|_||_|_|_|_| DD MMM YYYY
Maximum Intensity	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe
Causality/Relationship to investigational products: Is there a reasonable possibility that the AE may have been caused by the investigational product?					
Accd to KFDA standards	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown
Outcome	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae
Medically attended visit Refer to protocol for definition. If yes, specify type: HO : Hospitalisation ER : Emergency Room MD : Medical Personnel	[N] ☐ No [Y] ☐ Yes → type: |_|_| (HO/ER/MD)	[N] ☐ No [Y] ☐ Yes → type: |_|_| (HO/ER/MD)	[N] ☐ No [Y] ☐ Yes → type: |_|_| (HO/ER/MD)	[N] ☐ No [Y] ☐ Yes → type: |_|_| (HO/ER/MD)	[N] ☐ No [Y] ☐ Yes → type: |_|_| (HO/ER/MD)

gsk GlaxoSmithKline	Rota-070 (111700)	Center No.: I_I_I_I_I_I_I	Subject No.: I_I_I_I_I_I_I	Non Serious Adverse Event 2

NON SERIOUS ADVERSE EVENT (Continue from Non Serious Adverse Event 1)

AE no.	6	7	8	9	10
Description	______	______	______	______	______
For GSK					
Date Started	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY ☐ during immediate post-vaccination period(30 minutes)
Date Stopped	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY	I_I_I I_I_I_I I_I_I_I_I DD MMM YYYY
Maximum Intensity	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe	[1]☐ Mild [2]☐ Moderate [3]☐ Severe
Causality/Relationship to investigational products: Is there a reasonable possibility that the AE may have been caused by the investigational product?					
Accd to KFDA standards	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown	[1]☐Definitely related [2]☐Probably related [3]☐Possibly related [4]☐Probably not related [5]☐ Unknown
Outcome	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae	[1]☐Recovered / Resolved [2]☐Recovering / resolving [3]☐Not recovered/ not resolved [4]☐Recovered with sequelae /Resolved with sequelae
Medically attended visit Refer to protocol for definition. If yes, specify type: -HO : Hospitalisation -ER : Emergency Room -MD : Medical Personnel	[N]☐ No [Y]☐ Yes → type: I_I_I (HO/ER/MD)	[N]☐ No [Y]☐ Yes → type: I_I_I (HO/ER/MD)	[N]☐ No [Y]☐ Yes → type: I_I_I (HO/ER/MD)	[N]☐ No [Y]☐ Yes → type: I_I_I (HO/ER/MD)	[N]☐ No [Y]☐ Yes → type: I_I_I (HO/ER/MD)

GSK GlaxoSmithKline	Rota-070 (111700)	Center No.: |_|_|_|_|_|_|	Subject No.: |_|_|_|_|_|_|	Medication 1

CONCOMITANT MEDICATION

Have any medications/treatments been administered during 31 days after vaccination? ☐ No ☐ Yes, Complete the table below
Concomitant medication administered for the treatment of an AE or SAE within the follow-up period for adverse events must be recorded.
For prophylactic medication, treatments and/or medications specifically contraindicated, please refer to the protocol in section 6.9

MEDIC. AE - DRU

Trade/Generic Name	Medical Indication (Tick box if it is used as Prophylactic)		Total daily dose	Route*	Start and end date (DD MMM YYYY) (Tick box if continuing at end of study)		Is drugs used for treating AE?
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No
For GSK	For GSK	☐			Start: |_|_||_|_|_||_|_|_|_| End: |_|_||_|_|_||_|_|_|_|	☐	☐ Yes ☐ No

* Medication Route. Please Use below defined codes.

EXT	External	ID	Intradermal	IH	Inhalation	IM	Intramuscular	IR	Intraarticular	IT	Intrathecal	IV	Intravenous	PR	Rectal	VA	Vaginal
UNK	Unknown	PE	Parenteral	PO	Oral	IN	Intranasal	SC	Subcutaneous	SL	Sublingual	TD	Transdermal	TO	Topical	OTH	Other

GSK GlaxoSmithKline	Rota-070 (111700)	Center No : |_|_|_|_|_|_|	Subject No : |_|_|_|_|_|_|	CONCOMITANT VACCINATION

CONCOMITANT VACCINATION

Has any vaccine other than the study vaccine(s) been administered during 30 days prior and post vaccination?
☐No ☐Yes, please record concomitant vaccination with trade name and/or generic name, route and vaccine administration date

Trade/Generic Name	Route*	Administration date (DD MMM YYYY)	Trade/Generic Name	Route*	Administration date (DD MMM YYYY)
		|_|_||_|_|_||_|_|_|_|			|_|_||_|_|_||_|_|_|_|
For GSK			For GSK		
		|_|_||_|_|_||_|_|_|_|			|_|_||_|_|_||_|_|_|_|
For GSK			For GSK		
		|_|_||_|_|_||_|_|_|_|			|_|_||_|_|_||_|_|_|_|
For GSK			For GSK		
		|_|_||_|_|_||_|_|_|_|			|_|_||_|_|_||_|_|_|_|
For GSK			For GSK		
		|_|_||_|_|_||_|_|_|_|			|_|_||_|_|_||_|_|_|_|
For GSK			For GSK		
		|_|_||_|_|_||_|_|_|_|			|_|_||_|_|_||_|_|_|_|
For GSK			For GSK		

* Route	IN	Intranasal	TD	Transdermal	ID	Intradermal	IM	Intramuscular	SL	Sublingual	UNK	Unknown
Please Use codes defined next	IH	Inhalation	IV	Intravenous	PO	Oral	SC	Subcutaneous	PE	Parenteral	OTH	Other

STUDY CONCLUSION

Did the subject experience any Serious Adverse Event during the study period?
☐ No ☐ Yes → If yes, specify total number of SAEs.: |_|_|

Was the subject withdrawn from PMS? ☐ No ☐ Yes → Major reason for withdrawal (tick 1 box only)

- ☐ [SAE] Serious adverse event → Please complete and submit SAE report and specify SAE No. |_|_|
- ☐ [AEX] Non-Serious adverse event → Please complete Non-serious Adverse Event section & specify AE No. |_|_| or solicited AE code |_|_|
- ☐ [PTV] Protocol violation, please specify:______________________ / _For GSK______________________
- ☐ [CWS] Consent withdrawal, not due to an adverse event
- ☐ [MIG] Migrated / moved from the study area
- ☐ [LFU] Lost to follow-up
- ☐ [OTH] Other, please specify. ______________________ / _For GSK______________________

→ Who made the decision? [I] ☐ Investigator [P] ☐Parents/Guardians
→ Date of Last Contact: |_|_||_|_|_||_|_|_|_| (DD MMM YYYY)
→ Was the subject in good condition at date of last contact? ☐ Yes ☐ No, → please give details within the Adverse Events section

INVESTIGATOR'S SIGNATURE:

I confirm that I have reviewed the data in this Case Report Form for this subject. All information entered by myself or my colleagues is, to the best of my knowledge, complete and accurate, as of the date below

Investigator's signature: ______________________ Date: |_|_||_|_|_||_|_|_|_| (DD MMM YYYY)

Printed Investigators' name: ______________________

For GSK	Name of CRA:	Receipt Date: |_|_||_|_|_||_|_|_|_|

GSK GlaxoSmithKline	Rota-070 (111700)	Center No.: |_|_|_|_|_|_|	Subject No.: |_|_|_|_|_|_|	SAE Report Form

PMS : SAE Report Form ☐ Initial ☐ Follow-up (_______times)

Notification Date: \|__\|___\|____\| (DD MMM YYYY) GSK Receipt Date: \|__\|___\|____\| (DD MMM YYYY)

Patient Details

Center No: |_|_|_|_|_|_|	Source from : ☐ Hospitalization ☐ Out-patient ☐ ER AE. MA_TYPE. CODELIST. MA-TYPE_11170
Subject No: |_|_|_|_|_|_|	Gender : ☐ Male ☐ Female Date of Birth: |__|___|____| (DD MMM YYYY)

Medical history including drug allergic history: ____________________

Medication: (Please record all medication administered, and check on the suspected medication.)

Brand Name/Generic Name	Manufacturer	Daily dose	Frequency	Route	Start Date DD MMM YYYY	End Date DD MMM YYYY	Indication	Used previously?
					|__|___|____|	|__|___|____|		☐ Yes ☐ No
					|__|___|____|	|__|___|____|		☐ Yes ☐ No
					|__|___|____|	|__|___|____|		☐ Yes ☐ No
					|__|___|____|	|__|___|____|		☐ Yes ☐ No
					|__|___|____|	|__|___|____|		☐ Yes ☐ No

Information of Serious Adverse Event

Onset Date (DD/MMM/YYYY) : \|__\|___\|____\| AE. AE-SRDAT End Date (DD/MMM/YYYY) : \|__\|___\|____\| AE. AE-ERDAT ☐ Ongoing AE.ONGOING [new field]

Maximum Intensity: ☐ Mild ☐ Moderate ☐ Severe ☐ NA AE. AE_INTEN

Possible cause of SAE other than PMS product:
☐ Medical condition(s) ☐ Concomitant medication ☐ Activity related to study participation ☐ Other (Specify): ________

Description of SAE (Please provide a full description of SAE, patient status and treatment details): ________

AE. AE - DESC

Action & Outcome

Action taken with study medication as a result of the SAE:
☐ None ☐ Medication withdrawn ☐ Administration change (☐ Dosage ☐ Route ☐ Change to other medication)

Outcome : ☐ Natural Recovery _____ days from onset day ☐ Not Recovered ☐ Recovered with corrective treatment
☐ Unknown ☐ Recovering AE. DAY-ONST (new)

AE. OUTCOME codelist. OUTCOME_111700

SAE category : ☐ Results in death ☐ Life threatening ☐ Results in disability/incapacity ☐ Congenital anomaly/birth defect in the offspring
☐ Hospitalization or prolongation of hospitalization From \|__\|___\|____\| to \|__\|___\|____\| (DD MMM YYYY)

Was AE recurred when study medication is rechallanged? ☐ Yes ☐ No ☐ No rechallenge

AE. CAUSAL codelist: CAUSAL_REL_111700 → Relationship to study medication : ☐ Definitely related ☐ Probably related ☐ Possibly related ☐ Probably not related ☐ Unknown

Other comment: ________

Reporter

Name of investigator		Sign and Date	
Name of center		Tel No.	
Fax No.		E-Mail	

Demog GN 2 cols now ... codelist

N-PAR or PAR GN21102 or GN11D.

MEDICATION (Continue from Medication 1)

Trade/Generic Name	Medical Indication Tick box if it is used as Prophylactic		Total daily dose	Route*	Start and end date (DD MMM YYYY) Tick box if continuing at end of study		Is drugs used for treating AE?
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
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 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No
 For GSK	 For GSK	☐			Start: End:	☐	☐ Yes ☐ No

* Medication Route. Please Use below defined codes.

EXT	External	ID	Intradermal	IH	Inhalation	IM	Intramuscular	IR	Intraarticular	IT	Intrathecal	IV	Intravenous	PR	Rectal	VA	Vaginal
UNK	Unknown	PE	Parenteral	PO	Oral	IN	Intranasal	SC	Subcutaneous	SL	Sublingual	TD	Transdermal	TO	Topical	OTH	Other

WRITTEN INFORMED CONSENT FORM

Title: Safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea.

This post-marketing surveillance was requested by the Korean Food and Drug Administration. This surveillance is an observational process which doesn't affect routine medical practice. The human rotavirus vaccine (referred to as *Rotarix* ***or Rotarix liquid formulation (oral suspension or prefilled syringe)***) has been recently registered in Korea and ***at least*** 3000 subjects will take part in this surveillance. The purpose of this surveillance is to evaluate the safety (in terms of occurrence of any adverse event or serious adverse events) of the Korean infants aged 6 weeks and above at the time of the first dose of vaccination.

You are kindly requested to let your child/ward participate in this surveillance.

Please take time to read the following information carefully and discuss it if you wish with friends, relatives and your personal doctor and if you decided to let your child/ward to participate, please sign this consent form.

1. Safety Data Collection Procedure

If you decide to let your child/ward to participate, you will be requested to record any symptoms occurring between the day of the vaccine dose and the following 30 days in the diary card that will be given to you by the study doctor. You will need to return the completed diary card 30 days after your child/ward receives the vaccination. You will also be requested to promptly report to the doctor any occurrence of unexpected or serious adverse events after your child/ward receives the vaccine. The duration of the study will be approximately 3 months.

2. Voluntary Participation and Subjects Right to End Participation

Your child's/ward's participation in this surveillance is voluntary. You may refuse to let your child/ward to take part in this surveillance, or once in the surveillance you may decide to discontinue participation at any time. You must inform your study doctor if you decide to do this. Your decision not to let your child/ward to take part in the surveillance or to stop participating in the surveillance will not affect your child's/ward's current or future medical care, or any benefits to which your child/ward may otherwise be entitled.

3. Confidentiality and Data Privacy

If you decide to let your child/ward participate in the surveillance, the study doctor and staff will collect medical and personal information about your child/ward as part of doing the surveillance. GSK staff who sees this information at the site will keep it confidential.

The study site will also transfer to GSK some of the information it collects, in a coded form. The information transferred will not include your child's/ward's name, initials, address, or other direct identifiers. It will be assigned a code number that only the site can connect back to your child's/ward's name.

GSK Biologicals will keep the information and the results collected about your child/ward in this surveillance. Your child/ward's name and address are not included in the information kept by GSK Biologicals - only your doctor will keep this information.

By agreeing to take part in this surveillance, you will be allowing certain persons to see the information about your child/ward (including personal and other information) held by the study doctor. Your child's/ward's information will be looked at to confirm that it is correct and that it is related to your child/ward. This will be done by selected people working for GSK and the government regulatory authorities. These persons are required to maintain the confidentiality of your child's/ward's information. GSK Biologicals has told your doctor to keep the information about your child/ward in a secure place. GSK Biologicals will comply with internal procedures to protect personal and other information even in countries where data privacy laws are less strict than in Europe/US.

4. Foreseeable Risks or Inconvenience

Over 131, 000 infants have been enrolled in studies with GSK Biologicals' HRV vaccine (*Rotarix*). During these studies, over 53, 000 infants have received at least one dose of the vaccine.

As with any vaccine, unexpected illnesses (called serious adverse experiences), including allergic reactions to the vaccine, (itchy skin rash, shortness of breath and swelling of the face or tongue) may occur. Medical equipment necessary to treat any serious reactions to the study vaccine will be available at the site.

The following undesirable event has been observed to be common: (this may occur with up to 1 in 10 doses): diarrhoea.

The following undesirable events have been observed to be uncommon (these may occur with up to 1 in 100 doses): flatulence (gas), abdominal pain and dermatitis.

In rare cases (1 in 1000 doses of the vaccine) blood in stools has been observed.

GSK has identified the presence of material from PCV-1, a virus to which people are commonly exposed, in its Human Rotavirus Vaccine. There is no evidence that PCV-1 can infect humans or is harmful to humans. Based on these considerations and the extensive safety database available, the benefit/risk profile of GSK Biologicals' HRV vaccine has not changed and remains favourable.

5. Expected benefits

Infants who receive the *Rotarix* ***or Rotarix liquid formulation (oral suspension or prefilled syringe)*** vaccine may have the benefit of being protected against rotavirus disease.

Consent statement

Title: Safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ ***or Rotarix™ liquid formulation (oral suspension or prefilled syringe)*** when administered according to the prescribing information in Korea.

I confirm that I have understood the statements in the informed consent form and have had the opportunity to ask questions about this surveillance. Therefore I agree to let my child/ward take part in this surveillance. I will receive the full copy of the informed consent form referred to above, including this signed statement with my signature below.

Participant's Name:

Name of Parent/Guardian:

Signature of Parent/Guardian: **Date:**

Study Doctor's Name: **Date:**

Signature of Person conducting Consent:

Signature of principal or coordinating investigator

GlaxoSmithKline Biologicals

Global Clinical Research and Development

Investigator Approval Page

Please note that by signing this page, you take responsibility for the content of the clinical study report, including appendices

STUDY TITLE: Open, multi-centric, post-marketing surveillance (PMS) to monitor the reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.

Study: 111700 (Rota-070 PMS) Development Phase: PMS

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Name of Investigator: SON MOON SHIN

Affiliation /investigational centre: Cheil general hospital & women's healthcare center

Signature of Investigator: PPD PPD

Date: May 6, 2010

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22-APR-2010

GlaxoSmithKline Biologicals
Global Clinical Research and Development

Sponsor Signatory Approval Page

Please note that by signing this page, you take responsibility for the content of the clinical study report, including appendices

STUDY TITLE: Open, multi-centric, post-marketing surveillance (PMS) to monitor the reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to the prescribing information in Korea.

Study: 111700 (Rota-070 PMS) Development Phase: PMS

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Name of Sponsor Signatory:	Dr. Emilio Ledesma
Title of Sponsor Signatory:	Vice-President and Director Clinical R&D and Medical Affairs Asia Pacific.
Signature:	PPD
Date:	5 May 2010

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