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

Study No.: 102247 (ROTA-036)

Title: A phase IIIb, double-blind, randomized, placebo-controlled, multi-country and multi-center study to assess the efficacy, safety and immunogenicity of two doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine in healthy infants in co-administration with specific childhood vaccinations.

Rationale: The aim of the study was to evaluate the efficacy, immunogenicity and safety of 2 doses of the HRV vaccine in healthy infants when co-administered with specific childhood vaccinations in the European setting. The immunogenicity of childhood vaccinations† was also evaluated to explore any effect of co-administration with the HRV vaccine.
† Infanrix Hexa™ (DTPa-HBV- IPV/ Hib): GlaxoSmithKline (GSK) Biologicals' commercially available combined diphtheria, tetanus, acellular pertussis, Hepatitis B, *Haemophilus influenzae* type b and inactivated polio vaccine; Infanrix Polio Hib™ (DTPa-IPV/Hib): GSK Biologicals' commercially available combined diphtheria, tetanus, acellular pertussis and *Haemophilus influenzae* type b vaccine; Prevenar™ (7Pn): Wyeth Pharmaceuticals' commercially available 7-valent pneumococcal polysaccharide conjugate vaccine; Meningitec™ (MenC): Wyeth Pharmaceuticals' commercially available meningococcal group C conjugate vaccine.
This summary presents the efficacy data for the first efficacy follow-up period* and the HRV vaccine safety results. It also displays the immunogenicity data of HRV vaccine & of childhood vaccines, except for Finland and Italy.
*The first efficacy follow-up period: from 2 weeks after Dose 2 of study vaccination until study Month 8.
The results concerning the second & combined efficacy periods, the safety follow-up data during the second efficacy period and the immunogenicity of childhood vaccines in Finland and Italy are presented in CTRS rota-036 annex.

Phase: IIIb

Study Period: 08 September 2004 to 07 September 2005

Study Design: Double-blind, randomized (2:1), placebo-controlled, multi-center study with 2 parallel groups.

Centers: Multi-centre study conducted in 6 European countries with 13 study centers in the Czech Republic, 21 in Finland, 20 in France, 26 in Germany, 2 in Italy and 13 in Spain.

Indication: Immunization according to 0, 1 or 2-month schedule against rotavirus diseases in healthy infants aged 6 to 14 weeks at the time of the first dose.

Treatment: The treatment groups were as follows:

- HRV Group received the rotavirus vaccine,
- Placebo Group received a placebo.

Subjects in each group received 2 doses of HRV vaccine or placebo co-administered with the first 2 doses of the primary childhood vaccination series given according to the national plan of immunization in each country. The 3rd dose of the primary childhood vaccination series was administered according to the national plan of immunization in each country. DTPa-HBV-IPV/Hib was administered at 3, 4, 5 months of age in the Czech Republic; at 2, 3, 4 months of age in France (DTPa-IPV/Hib given at Dose 2) and Germany; at 2, 4, 6 months of age in Spain; at 3, 5, 11-12# months of age in Finland; at 3, 5, 11# months of age in Italy. MenC was co-administered in Spain; 7Pn was co-administered in France and Germany.
Administration of Dose 3 of the primary childhood vaccinations in Finland and Italy took place beyond the follow-up period of this study.
Note: Visits 1 to 3 corresponded to study Months 0, 1 or 2 and 3 or 4, respectively, Visit 4 (in Spain only) corresponded to Month 5 and Visit 5 was planned mid-June to mid-July 2006

Objectives: To determine the efficacy of two doses of GSK Biologicals' HRV vaccine given concomitantly with specific childhood vaccinations against any rotavirus (RV) gastroenteritis (GE) caused by the circulating wild-type RV strains during the first efficacy follow-up period.

Primary Outcome/Efficacy Variable:
Occurrence of any RV GE caused by the circulating wild-type RV strains during the first efficacy follow-up period.

Secondary Outcome/Efficacy Variable(s):
Efficacy:
During the first efficacy follow-up period:

- Occurrence of severe RV GE caused by the circulating wild-type RV strains.
- Occurrence of any and severe RV GE caused by the circulating wild-type RV strains of G1 type.
- Occurrence of any and severe RV GE caused by the circulating wild-type RV strains of non-G1 types.
- Occurrence of hospitalization due to RV GE caused by the circulating wild-type RV strains.

- Occurrence of any medical attention (medical provider contact, advice, visit; emergency room contact or visit or hospitalization) for RV GE caused by the circulating wild-type RV strains.
- Occurrence of any and severe RV GE caused by the circulating wild-type RV strains during the period starting from Dose 1 of the study vaccine until Visit 5.
- Occurrence of any and severe RV GE caused by the circulating wild-type RV strains in subjects who completed the two-dose vaccination course before the RV epidemic season*.
- Occurrence of any and severe RV GE caused by the circulating wild-type RV strains in subjects who were vaccinated during the RV epidemic season*.

*Not evaluated as almost all subjects were vaccinated during the RV epidemic season.

Immunogenicity (in a subset of subjects, planned N=1800):

- Serum anti-rotavirus immunoglobulin A (IgA) antibody concentration expressed as geometric mean concentration (GMC) at Visit 1 and Visit 3.
- Seroconversion rates to anti-rotavirus IgA antibody at Visit 3. Seroconversion was defined as the appearance of anti-rotavirus IgA antibody concentration ≥ 20 U/mL in subjects initially (i.e. prior to the first dose of HRV vaccine or placebo) seronegative for rotavirus.
- Serum levels of antibodies to all antigens contained in each of the different childhood vaccinations at Visit 3 and Visit 4:
    - Serum concentration/titer expressed as GMC/geometric mean antibody titer (GMT) for antibodies against diphtheria, tetanus, pertussis toxoid (PT), filamentous haemagglutinin (FHA), pertactin (PRN), poliovirus types 1, 2 and 3, polyribosyl ribitol phosphate (PRP), hepatitis B surface antigen (HBs), serum bactericidal activity against *Neisseria meningitidis* serogroup C (SBA-Men C), polysaccharide C (PSC), and *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F.
    - Seroprotection status, defined as:
        - Anti-diphtheria and anti-tetanus antibody concentrations ≥ 0.1 IU/mL
        - Anti-poliovirus types 1, 2 and 3 antibody titers ≥ 8
        - Anti-PRP antibody concentrations ≥ 0.15 μg/mL and ≥ 1.0 μg/mL
        - Anti-HBs antibody concentrations ≥ 10.0 mIU/mL
    - Seropositivity status, defined as:
        - Anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5 EL.U/mL
        - SBA-MenC antibody titer ≥ 1/8
        - Anti-PSC antibody concentrations (ELISA) ≥ 0.3 μg/mL
        - Antibody concentrations to *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F ≥ 0.05 μg/mL

Safety:

- In a subset of subjects (planned N=1800), occurrence of each type of solicited symptom within the 8-day (Day 0-7) solicited follow-up period after each dose of HRV vaccine or placebo co-administered with childhood vaccinations.
- For all subjects, occurrence of unsolicited adverse events (AEs) within 31 days (Day 0-30) after each dose of HRV vaccine or placebo co-administered with childhood vaccinations, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- For all subjects, occurrence of serious adverse events (SAEs) throughout the entire study period.

Statistical Methods:

The analyses were performed on the Total Vaccinated Cohort, the Total Vaccinated Cohort for the immunogenicity and safety subset, the According-To-Protocol (ATP) cohort for efficacy and the ATP cohort for immunogenicity.

The Total Vaccinated Cohort included all subjects with at least one study vaccine administration documented.

The Total Vaccinated Cohort for the immunogenicity and safety subset included all subjects with at least one study vaccine administration documented and for whom solicited symptoms and blood samples were to be collected.

The ATP cohort for efficacy included all subjects:

- who received 2 doses of HRV vaccine or placebo according to their random assignment,
- who had entered into the efficacy surveillance period: had follow-up beyond 2 weeks after Dose 2 of study vaccination for the analysis of the first efficacy follow-up period,
- who had no RV other than vaccine strain in GE stool samples collected between the day on which Dose 1 was administered and 2 weeks after Dose 2 of HRV vaccine or placebo was administered,
- for whom the randomization code had not been broken,
- who had not received a vaccine forbidden by or not specified in the protocol,
- who were seronegative for serum anti-rotavirus IgA antibodies on the day of Dose 1 of HRV vaccine or placebo for subjects included in the immunogenicity and safety subset,

- who had not received a replacement vial, except if the appropriate vaccine was administered in double-blind replacement.

The ATP cohort for immunogenicity included all subjects:

- who had received at least one dose of study vaccine/control according to their random assignment,
- for whom the randomization code had not been broken,
- who had not received a replacement vial, except if the appropriate vaccine was administered in double-blind replacement,
- who had not received a vaccine forbidden by or not specified in the protocol,
- who were seronegative for serum anti-rotavirus IgA antibodies on the day of Dose 1 of HRV vaccine or placebo,
- who had not received medication forbidden by the protocol,
- whose underlying medical condition was not forbidden by the protocol,
- with no protocol violation of demographics (unknown age at study entry or outside protocol defined age-interval),
- who complied with vaccination schedule for HRV vaccine or placebo,
- who complied with blood sampling schedule,
- for whom immunogenicity data were available, at pre- and post-sampling time point for anti-rotavirus IgA antibody,
- who had no RV other than the vaccine strain in GE stool samples collected up to Visit 3,
- who had no concomitant infection unrelated to the vaccine which might have influenced the immune response.

Analysis of efficacy

Analysis of efficacy for the first efficacy period was performed on the ATP cohort for efficacy. Analysis of efficacy from the first dose onwards was performed on the Total Vaccinated Cohort.

Only GE episodes in which wild-type RV (i.e. other than the vaccine strain) was identified in a stool specimen were included in the efficacy analysis. Number of GE episodes and RV GE episodes reported during the first efficacy period, by severity using the 20-point Vesikari scale was presented for pooled countries. The Vaccine Efficacy (VE) estimates were calculated with 95% Confidence Interval (CI) for the required efficacy variables for each Group.

The VE was defined as the percentage reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo. This was calculated as follows:

VE = 1 – (ARV/ARU)

where:

ARU = disease attack rate in the unvaccinated population (estimated from the Placebo Group) = nu/Nu = the number of subjects with at least one RV GE episode divided by the total number of subjects in the Placebo group.

ARV = disease attack rate in the vaccinated group = nv/Nv = the number of subjects with at least one RV GE episode divided by the total number of subjects in the HRV Group.

ARV/ARU= Relative Risk (RR)

Analysis of immunogenicity

The analysis was performed on the ATP cohort for immunogenicity.

GMCs and seroconversion rates for anti-rotavirus IgA antibodies were calculated with their 95% CIs for each group at Visits 1 & 3 for all countries and at Visit 4 for Spain only. GMCs/GMTs and seropositivity/seroprotection rates for antibodies against co-administered vaccine antigens were calculated with their 95% CIs for each group at post-Dose 3 per country.

Analysis of safety

The analysis was performed on the Total Vaccinated Cohort for the immunogenicity and safety subset.

The percentage of subjects, with their exact 95% CI, with each individual solicited general symptom, symptoms considered as related to the vaccine and symptoms of grade 3 in intensity, during the 8-day (Day 0-7) solicited follow-up period was tabulated for each group, after each dose. For all subjects, the percentage of subjects with unsolicited AEs within 31 days (Day 0-30) after each dose was summarized by group, for pooled countries, according to the Medical Dictionary for regulatory activities (MedDRA) preferred terms. The percentage of subjects with SAEs during the entire study period was tabulated per group according to MedDRA preferred terms.

Study Population: Healthy infants with birth weight > 2000 g who were 6-14 weeks of age at the time of the first dose of HRV vaccine or placebo, free of obvious health problems as established by medical history and clinical examination before entering into the study. Written informed consent was obtained from parents or guardians before any study-specific procedures were performed.

Number of Subjects	HRV Group	Placebo Group
Planned, N	2660	1330
Randomized, N (Total Vaccinated Cohort)	2646	1348
Completed, n (%)	2613 (98.8)	1331 (98.7)
Total Number Subjects Withdrawn, n (%)	33 (1.2)	17 (1.3)

Withdrawn due to Adverse Events, n (%)	7 (0.3)	6 (0.4)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	26 (1.0)	11 (0.8)
Demographics	HRV Group	Placebo Group
N (Total Vaccinated Cohort)	2646	1348
Females:Males	1230:1416	657:691
Mean Age, weeks (SD)	11.5 (1.81)	11.4 (1.84)
White/Caucasian, n (%)	2604 (98.4)	1323 (98.1)

Primary Efficacy Results:
Percentage of subjects with any RV GE episodes and vaccine efficacy from 2 weeks after Dose 2 up to Visit 5 (ATP cohort for efficacy)

Group	N	n	n/N			Vaccine Efficacy		
			%	95% CI		%	95% CI	
				LL	UL		LL	UL
HRV	2572	24	0.9	0.6	1.4	87.1	79.6	92.1
Placebo	1302	94	7.2	5.9	8.8	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects with at least one RV GE episode caused by the circulating wild-type RV
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit

Secondary Outcome Variable(s):
Percentage of subjects with severe (Vesikari score $\geq$ 11 points) RV GE episodes and vaccine efficacy from 2 weeks after Dose 2 up to Visit 5 (ATP cohort for efficacy)

Group	N	n	n/N			Vaccine Efficacy		
			%	95% CI		%	95% CI	
				LL	UL		LL	UL
HRV	2572	5	0.2	0.1	0.5	95.8	89.6	98.7
Placebo	1302	60	4.6	3.5	5.9	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects with at least one severe RV GE episode caused by the circulating wild-type RV
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit

Secondary Outcome Variable(s):
Percentage of subjects with any RV GE episodes and vaccine efficacy from 2 weeks after Dose 2 up to Visit 5, by RV type (ATP cohort for efficacy)

Group	N	n	n/N			Vaccine Efficacy		
			%	95% CI		%	95% CI	
				LL	UL		LL	UL
G1 wild-type								
HRV	2572	4	0.2	0.0	0.4	95.6	87.9	98.8
Placebo	1302	46†	3.5	2.6	4.7	-	-	-
Pooled Non-G1 (G2, G3, G4, G9)								
HRV	2572	20	0.8	0.5	1.2	79.3	64.6	88.4
Placebo	1302	49	3.8	2.8	4.9	-	-	-
G2								
HRV	2572	3	0.1	0.0	0.3	62.0	-124.4	94.4
Placebo	1302	4	0.3	0.1	0.8	-	-	-
G3								
HRV	2572	1	0.0	0.0	0.2	89.9	9.5	99.8
Placebo	1302	5	0.4	0.1	0.9	-	-	-
G4								
HRV	2572	3	0.1	0.0	0.3	88.3	57.5	97.9
Placebo	1302	13†	1.0	0.5	1.7	-	-	-
G9								
HRV	2572	13	0.5	0.3	0.9	75.6	51.1	88.5
Placebo	1302	27	2.1	1.4	3.0	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects with at least one specified RV GE episode in each group

95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit
† One subject from the Placebo Group was counted in G1 and G4 categories since both RV types were isolated.

Secondary Outcome Variable(s):
Percentage of subjects with severe (Vesikari score ≥ 11) RV GE episodes and vaccine efficacy from 2 weeks after Dose 2 up to Visit 5, by RV type (ATP cohort for efficacy)

Group	N	n	n/N			Vaccine Efficacy		
			%	95% CI		%	95% CI	
				LL	UL		LL	UL
G1 wild-type								
HRV	2572	2	0.1	0.0	0.3	96.4	85.7	99.6
Placebo	1302	28†	2.2	1.4	3.1	-	-	-
Pooled Non-G1 (G2, G3, G4, G9)								
HRV	2572	3	0.1	0.0	0.3	95.4	85.3	99.1
Placebo	1302	33	2.5	1.8	3.5	-	-	-
G2								
HRV	2572	1	0.0	0.0	0.2	74.7	-386.2	99.6
Placebo	1302	2	0.2	0.0	0.6	-	-	-
G3								
HRV	2572	0	0.0	0.0	0.1	100	44.8	100
Placebo	1302	5	0.4	0.1	0.9	-	-	-
G4								
HRV	2572	0	0.0	0.0	0.1	100	64.9	100
Placebo	1302	7†	0.5	0.2	1.1	-	-	-
G9								
HRV	2572	2	0.1	0.0	0.3	94.7	77.9	99.4
Placebo	1302	19	1.5	0.9	2.3	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects with at least one specified severe RV GE episode in each group
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit
† One subject from the Placebo Group counted in G1 and G4 categories since both RV types were isolated.

Secondary Outcome Variable(s):
Percentage of subjects hospitalized due to RV GE episodes and vaccine efficacy from 2 weeks after Dose 2 up to Visit 5 (ATP cohort for efficacy)

Group	N	n	n/N			Vaccine Efficacy		
			%	95% CI		%	95% CI	
				LL	UL		LL	UL
HRV	2572	0	0.0	0.0	0.1	100	81.8	100
Placebo	1302	12	0.9	0.5	1.6	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects hospitalized due to RV GE episode caused by the circulating wild-type RV
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit

Secondary Outcome Variable(s):
Percentage of subjects with RV GE requiring medical attention and vaccine efficacy from 2 weeks after Dose 2 up to Visit 5 (ATP cohort for efficacy)

Group	N	n	n/N			Vaccine Efficacy		
			%	95% CI		%	95% CI	
				LL	UL		LL	UL
HRV	2572	10	0.4	0.2	0.7	91.8	84.0	96.3
Placebo	1302	62	4.8	3.7	6.1	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects with at least one RV GE episode caused by the circulating wild-type RV with medical attention in each group
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit

Secondary Outcome Variable(s):
Percentage of subjects with any RV GE episodes and vaccine efficacy from Dose 1 up to Visit 5 (Total Vaccinated Cohort)

Group	N	n	n/N	Vaccine Efficacy

			%	95% CI		%	95% CI	
				LL	UL		LL	UL
HRV	2646	26	1.0	0.6	1.4	87.3	80.3	92.0
Placebo	1348	104	7.7	6.3	9.3	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects with at least one RV GE episode caused by the circulating wild-type RV
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit

Secondary Outcome Variable(s):
Percentage of subjects with severe (Vesikari score $\geq$ 11) RV GE episodes and vaccine efficacy from Dose 1 up to Visit 5 (Total Vaccinated Cohort)

Group	N	n	n/N			Vaccine Efficacy		
			%	95% CI		%	95% CI	
				LL	UL		LL	UL
HRV	2646	5	0.2	0.1	0.4	96.0	90.2	98.8
Placebo	1348	64	4.7	3.7	6.0	-	-	-

N = number of subjects included in each group
n (%) = number (percentage) of subjects with at least one severe RV GE episode caused by the circulating wild-type RV
95% CI = 95% confidence interval; LL = Lower Limit; UL = Upper Limit

Secondary Outcome Variable(s):
Seroconversion rates and GMCs for anti-rotavirus IgA antibodies (ATP cohort for immunogenicity)

Country	Group	Timing	N	≥ 20 U/mL				GMC (U/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
All	HRV	PRE	794	0	0.0	0.0	0.5	< 20	-	-
		PII(M3-M4)	787	681	86.5	83.9	88.8	197.2	175.2	222.0
		PII(M5)	184	152	82.6	76.3	87.8	113.3	90.8	141.5
	Placebo	PRE	422	0	0.0	0.0	0.9	< 20	-	-
		PII(M3-M4)	420	28	6.7	4.5	9.5	< 20	-	-
		PII(M5)	90	14	15.6	8.8	24.7	< 20	-	-
Czech Republic	HRV	PRE	182	0	0.0	0.0	2.0	< 20	-	-
		PII(M3-M4)	182	154	84.6	78.5	89.5	152.5	118.9	195.4
	Placebo	PRE	90	0	0.0	0.0	4.0	< 20	-	-
		PII(M3-M4)	90	2	2.2	0.3	7.8	< 20	-	-
Finland	HRV	PRE	167	0	0.0	0.0	2.2	< 20	-	-
		PII(M3-M4)	167	158	94.6	90.0	97.5	412.2	325.9	521.2
	Placebo	PRE	105	0	0.0	0.0	3.5	< 20	-	-
		PII(M3-M4)	105	3	2.9	0.6	8.1	< 20	-	-
France	HRV	PRE	83	0	0.0	0.0	4.3	< 20	-	-
		PII(M3-M4)	83	70	84.3	74.7	91.4	181.8	126.4	261.6
	Placebo	PRE	43	0	0.0	0.0	8.2	< 20	-	-
		PII(M3-M4)	43	6	14.0	5.3	27.9	< 20	-	-
Germany	HRV	PRE	156	0	0.0	0.0	2.3	< 20	-	-
		PII(M3-M4)	156	128	82.1	75.1	87.7	166.0	126.0	218.9
	Placebo	PRE	84	0	0.0	0.0	4.3	< 20	-	-
		PII(M3-M4)	84	5	6.0	2.0	13.3	< 20	-	-
Italy	HRV	PRE	13	0	0.0	0.0	24.7	< 20	-	-
		PII(M3-M4)	13	12	92.3	64.0	99.8	205.1	80.5	522.7
	Placebo	PRE	9	0	0.0	0.0	33.6	< 20	-	-
		PII(M3-M4)	9	1	11.1	0.3	48.2	< 20	-	-
Spain	HRV	PRE	193	0	0.0	0.0	1.9	< 20	-	-
		PII(M3-M4)	186	159	85.5	79.6	90.2	156.3	123.4	198.0
		PII(M5)	184	152	82.6	76.3	87.8	113.3	90.8	141.5
	Placebo	PRE	91	0	0.0	0.0	4.0	< 20	-	-
		PII(M3-M4)	89	11	12.4	6.3	21.0	< 20	-	-
		PII(M5)	90	14	15.6	8.8	24.7	< 20	-	-

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination
PII(M3-M4) = blood sample taken 1 to 2 months after Dose 2 of HRV vaccine or placebo
PII(M5) = blood sample taken 3 months after Dose 2 of HRV vaccine or placebo

Secondary Outcome Variable(s):
Seropositivity rates and GMTs for anti-SBA-MenC antibodies post-Dose 3 of MenC for Spain (ATP cohort for immunogenicity)

Group	N	≥ 1:8 dilution				≥ 1:128 dilution				GMT		
		n	%	95% CI		n	%	95% CI		Value	95% CI	
				LL	UL			LL	UL		LL	UL
HRV	184	184	100	98.0	100	181	98.4	95.3	99.7	1455.4	1240.2	1707.9
Placebo	90	90	100	96.0	100	90	100	96.0	100	1769.1	1374.3	2277.5

N = number of subjects with available results
n (%) = number (percentage) of subjects with titer ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s):
Seropositivity rates and GMCs for anti-PSC antibodies post-Dose 3 of MenC for Spain (ATP cohort for immunogenicity)

Group	N	≥ 0.3 μg/mL				≥ 2.0 μg/mL				GMC (μg/mL)		
		n	%	95% CI		n	%	95% CI		Value	95% CI	
				LL	UL			LL	UL		LL	UL
HRV	187	187	100	98.0	100	183	97.9	94.6	99.4	7.63	6.81	8.55
Placebo	91	91	100	96.0	100	88	96.7	90.7	99.3	8.76	7.56	10.15

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s):
Seropositivity rates and GMCs for antibodies to *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F post-Dose 3 of 7Pn (ATP cohort for immunogenicity)

Serotype	Country	Group	N	≥ 0.05 μg/mL				≥ 0.2 μg/mL				GMC (μg/mL)		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
4	France	HRV	83	83	100	95.7	100	83	100	95.7	100	2.40	2.02	2.85
		Placebo	43	43	100	91.8	100	43	100	91.8	100	2.39	2.02	2.83
	Germany	HRV	155	155	100	97.6	100	155	100	97.6	100	3.17	2.80	3.59
		Placebo	84	84	100	95.7	100	84	100	95.7	100	3.11	2.56	3.78
6B	France	HRV	83	80	96.4	89.8	99.2	69	83.1	73.3	90.5	0.79	0.59	1.07
		Placebo	43	42	97.7	87.7	99.9	38	88.4	74.9	96.1	0.65	0.46	0.93
	Germany	HRV	155	138	89.0	83.0	93.5	107	69.0	61.1	76.2	0.48	0.37	0.63
		Placebo	84	77	91.7	83.6	96.6	59	70.2	59.3	79.7	0.49	0.35	0.70
9V	France	HRV	83	83	100	95.7	100	83	100	95.7	100	2.42	2.06	2.84
		Placebo	43	43	100	91.8	100	43	100	91.8	100	2.39	2.00	2.86
	Germany	HRV	155	155	100	97.6	100	154	99.4	96.5	100	2.94	2.57	3.36
		Placebo	84	84	100	95.7	100	84	100	95.7	100	2.65	2.13	3.29
14	France	HRV	83	83	100	95.7	100	83	100	95.7	100	4.68	3.75	5.84
		Placebo	43	43	100	91.8	100	43	100	91.8	100	5.29	4.22	6.63
	Germany	HRV	155	155	100	97.6	100	154	99.4	96.5	100	4.59	3.93	5.37
		Placebo	84	84	100	95.7	100	83	98.8	93.5	100	3.89	2.99	5.08
18C	France	HRV	83	81	97.6	91.6	99.7	80	96.4	89.8	99.2	2.47	1.92	3.18
		Placebo	43	43	100	91.8	100	43	100	91.8	100	2.56	2.03	3.24
	Germany	HRV	155	155	100	97.6	100	154	99.4	96.5	100	3.40	2.89	4.01
		Placebo	84	84	100	95.7	100	82	97.6	91.7	99.7	3.31	2.62	4.19
19F	France	HRV	83	83	100	95.7	100	81	97.6	91.6	99.7	2.85	2.30	3.52
		Placebo	43	43	100	91.8	100	42	97.7	87.7	99.9	2.75	2.05	3.69

	Germany	HRV	155	155	100	97.6	100	154	99.4	96.5	100	3.62	3.06	4.27
		Placebo	84	84	100	95.7	100	84	100	95.7	100	3.51	2.87	4.29
23F	France	HRV	83	82	98.8	93.5	100	76	91.6	83.4	96.5	1.25	0.95	1.65
		Placebo	43	43	100	91.8	100	41	95.3	84.2	99.4	1.35	1.01	1.80
	Germany	HRV	155	147	94.8	90.1	97.7	137	88.4	82.3	93.0	1.31	1.03	1.68
		Placebo	84	80	95.2	88.3	98.7	71	84.5	75.0	91.5	1.21	0.84	1.75

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s):
Seroprotection rates and GMCs for anti-diphtheria and anti-tetanus antibodies post-Dose 3 of childhood vaccinations (ATP cohort for immunogenicity)

Antibody	Country	Group	N	≥ 0.1 IU/mL				GMC (IU/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
Anti-diphtheria	Czech Republic	HRV	182	182	100	98.0	100	2.321	2.097	2.569
		Placebo	89	89	100	95.9	100	2.694	2.292	3.165
	France	HRV	83	83	100	95.7	100	1.168	0.963	1.417
		Placebo	43	43	100	91.8	100	1.118	0.838	1.490
	Germany	HRV	155	148	95.5	90.9	98.2	1.389	1.140	1.694
		Placebo	84	83	98.8	93.5	100	1.350	1.058	1.723
	Spain	HRV	188	188	100	98.1	100	6.653	6.077	7.284
		Placebo	91	91	100	96.0	100	6.830	5.865	7.953
Anti-tetanus	Czech Republic	HRV	182	182	100	98.0	100	1.918	1.690	2.177
		Placebo	90	90	100	96.0	100	1.789	1.499	2.136
	France	HRV	83	83	100	95.7	100	1.353	1.126	1.627
		Placebo	43	43	100	91.8	100	1.384	1.112	1.723
	Germany	HRV	155	152	98.1	94.4	99.6	1.094	0.919	1.302
		Placebo	84	84	100	95.7	100	1.150	0.924	1.430
	Spain	HRV	188	187	99.5	97.1	100	1.665	1.469	1.888
		Placebo	90	90	100	96.0	100	1.669	1.408	1.978

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s):
Seropositivity rates and GMCs for anti-PT, anti-FHA and anti-PRN antibodies post-Dose 3 of childhood vaccinations (ATP cohort for immunogenicity)

Antibody	Country	Group	N	≥ 5 EL.U/mL				GMC (EL.U/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
Anti-PT	Czech Republic	HRV	181	180	99.4	97.0	100	55.6	50.6	61.0
		Placebo	90	90	100	96.0	100	53.4	46.5	61.3
	France	HRV	83	83	100	95.7	100	42.1	37.2	47.8
		Placebo	43	43	100	91.8	100	46.3	39.3	54.5
	Germany	HRV	153	140	91.5	85.9	95.4	30.2	25.7	35.5
		Placebo	82	77	93.9	86.3	98.0	28.4	23.2	34.7
	Spain	HRV	188	187	99.5	97.1	100	42.9	39.0	47.2
		Placebo	91	91	100	96.0	100	45.1	40.3	50.5
Anti-FHA	Czech Republic	HRV	182	182	100	98.0	100	215.8	196.4	237.2
		Placebo	90	90	100	96.0	100	214.8	188.2	245.1
	France	HRV	82	82	100	95.6	100	176.2	153.4	202.4
		Placebo	43	43	100	91.8	100	180.3	152.5	213.0
	Germany	HRV	155	152	98.1	94.4	99.6	110.3	90.3	134.8
		Placebo	84	82	97.6	91.7	99.7	97.5	74.7	127.3
	Spain	HRV	188	188	100	98.1	100	159.2	144.6	175.3

		Placebo	91	91	100	96.0	100	161.1	141.8	183.1
Anti-PRN	Czech Republic	HRV	182	182	100	98.0	100	112.8	100.5	126.7
		Placebo	90	90	100	96.0	100	113.8	97.0	133.5
	France	HRV	82	82	100	95.6	100	101.4	85.2	120.8
		Placebo	43	43	100	91.8	100	110.7	82.5	148.7
	Germany	HRV	155	147	94.8	90.1	97.7	73.6	59.8	90.6
		Placebo	84	82	97.6	91.7	99.7	75.6	57.2	100.0
	Spain	HRV	188	188	100	98.1	100	105.3	94.3	117.5
		Placebo	91	91	100	96.0	100	106.7	89.7	126.9

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s):
Seroprotection rates and GMCs for anti-HBs antibodies post-Dose 3 of childhood vaccinations (ATP cohort for immunogenicity)

Country	Group	Timing	N	≥ 10 mIU/mL				GMC (mIU/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
Czech Republic	HRV	PIII(M3-M5)	181	177	97.8	94.4	99.4	408.6	330.2	505.6
	Placebo	PIII(M3-M5)	90	88	97.8	92.2	99.7	329.4	248.7	436.4
France	HRV	PII(M3-M4)	80	77	96.3	89.4	99.2	401.4	281.9	571.7
	Placebo	PII(M3-M4)	43	42	97.7	87.7	99.9	481.9	290.9	798.3
Germany	HRV	PIII(M3-M5)	152	119	78.3	70.9	84.6	143.2	102.1	200.8
	Placebo	PIII(M3-M5)	82	65	79.3	68.9	87.4	117.7	76.5	181.0
Spain	HRV	PIII(M3-M5)	187	184	98.4	95.4	99.7	832.5	676.2	1025.0
	Placebo	PIII(M3-M5)	90	85	94.4	87.5	98.2	861.3	589.6	1258.2

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M3-M5) = post-HBV childhood vaccination dose 3 (Visit 3 for Czech Republic and Germany; Visit 4 for Spain)
PII(M3-M4) = post-HBV childhood vaccination dose 2 (Visit 3 for France)

Secondary Outcome Variable(s):
Seroprotection rates and GMTs for anti-poliovirus types 1, 2 and 3 antibodies post-Dose 3 of childhood vaccinations (ATP cohort for immunogenicity)

Anti-poliovirus	Country	Group	N	≥ 8				GMT		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
Type 1	Czech Republic	HRV	122	122	100	97.0	100	445.5	343.4	578.0
		Placebo	65	65	100	94.5	100	370.0	274.2	499.2
	France	HRV	44	44	100	92.0	100	89.7	58.9	136.6
		Placebo	30	29	96.7	82.8	99.9	142.3	75.5	268.3
	Germany	HRV	108	99	91.7	84.8	96.1	119.1	82.0	173.0
		Placebo	60	55	91.7	81.6	97.2	85.4	54.7	133.3
	Spain	HRV	123	123	100	97.0	100	661.7	533.0	821.5
		Placebo	58	58	100	93.8	100	590.9	438.6	796.2
Type 2	Czech Republic	HRV	124	124	100	97.1	100	376.5	288.7	491.1
		Placebo	59	57	96.6	88.3	99.6	269.8	173.1	420.6
	France	HRV	44	41	93.2	81.3	98.6	52.5	33.2	82.8
		Placebo	29	27	93.1	77.2	99.2	49.8	26.5	93.4
	Germany	HRV	110	92	83.6	75.4	90.0	62.0	43.1	89.1
		Placebo	62	51	82.3	70.5	90.8	51.7	32.6	82.2
	Spain	HRV	118	117	99.2	95.4	100	402.6	310.7	521.8
		Placebo	57	57	100	93.7	100	267.1	185.0	385.6
Type 3	Czech Republic	HRV	114	114	100	96.8	100	1153.0	884.4	1503.1
		Placebo	65	65	100	94.5	100	970.6	696.6	1352.5

	France	HRV	44	44	100	92.0	100	217.3	128.9	366.1
		Placebo	30	30	100	88.4	100	189.8	101.6	354.6
	Germany	HRV	109	98	89.9	82.7	94.9	211.5	138.1	323.9
		Placebo	59	52	88.1	77.1	95.1	107.2	60.8	189.1
	Spain	HRV	120	117	97.5	92.9	99.5	1126.3	854.2	1485.2
		Placebo	53	53	100	93.3	100	880.8	596.0	1301.8

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody titer ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s):
Seroprotection rates and GMCs for anti-PRP antibodies post-Dose 3 of childhood vaccinations (ATP cohort for immunogenicity)

Country	Group	N	≥ 0.15 µg/mL				≥ 1.0 µg/mL				GMC (µg/mL)		
			n	%	95% CI		n	%	95% CI		Value	95% CI	
					LL	UL			LL	UL		LL	UL
Czech Republic	HRV	182	179	98.4	95.3	99.7	139	76.4	69.5	82.3	2.862	2.349	3.486
	Placebo	90	90	100	96.0	100	65	72.2	61.8	81.1	2.264	1.746	2.937
France	HRV	80	76	95.0	87.7	98.6	46	57.5	45.9	68.5	1.388	1.006	1.916
	Placebo	43	42	97.7	87.7	99.9	26	60.5	44.4	75.0	1.385	0.955	2.007
Germany	HRV	154	133	86.4	79.9	91.4	93	60.4	52.2	68.2	1.344	1.028	1.757
	Placebo	83	68	81.9	72.0	89.5	50	60.2	48.9	70.8	1.098	0.751	1.604
Spain	HRV	187	182	97.3	93.9	99.1	148	79.1	72.6	84.7	2.796	2.268	3.447
	Placebo	91	85	93.4	86.2	97.5	71	78.0	68.1	86.0	2.607	1.873	3.630

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration ≥ the specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s):
Percentage of subjects with solicited general symptoms reported during the 8-day (Day 0-7) follow-up period after each HRV vaccine/placebo dose for pooled countries (Total Vaccinated Cohort for the immunogenicity and safety subset)

Symptom	Intensity / relationship	HRV Group					Placebo Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Dose 1											
Cough/ Runny nose	Any	914	221	24.2	21.4	27.1	490	117	23.9	20.2	27.9
	Grade 3	914	7	0.8	0.3	1.6	490	2	0.4	0.0	1.5
	Related	914	58	6.3	4.9	8.1	490	29	5.9	4.0	8.4
Diarrhea	Any	914	24	2.6	1.7	3.9	490	11	2.2	1.1	4.0
	Grade 3	914	3	0.3	0.1	1.0	490	4	0.8	0.2	2.1
	Related	914	18	2.0	1.2	3.1	490	7	1.4	0.6	2.9
Fever (axillary)	≥ 37.5 °C	914	166	18.2	15.7	20.8	490	91	18.6	15.2	22.3
	> 39.0 °C	914	0	0.0	0.0	0.4	490	0	0.0	0.0	0.8
	Related	914	133	14.6	12.3	17.0	490	67	13.7	10.8	17.0
Irritability/ Fussiness	Any	914	460	50.3	47.0	53.6	490	250	51.0	46.5	55.5
	Grade 3	914	23	2.5	1.6	3.8	490	19	3.9	2.4	6.0
	Related	914	299	32.7	29.7	35.9	490	171	34.9	30.7	39.3
Loss of appetite	Any	914	210	23.0	20.3	25.8	490	100	20.4	16.9	24.3
	Grade 3	914	4	0.4	0.1	1.1	490	1	0.2	0.0	1.1
	Related	914	126	13.8	11.6	16.2	490	71	14.5	11.5	17.9
Vomiting	Any	914	101	11.1	9.1	13.3	490	52	10.6	8.0	13.7
	Grade 3	914	10	1.1	0.5	2.0	490	6	1.2	0.5	2.6
	Related	914	44	4.8	3.5	6.4	490	24	4.9	3.2	7.2
Dose 2											
Cough/ Runny nose	Any	905	234	25.9	23.0	28.8	486	149	30.7	26.6	35.0
	Grade 3	905	10	1.1	0.5	2.0	486	1	0.2	0.0	1.1
	Related	905	53	5.9	4.4	7.6	486	34	7.0	4.9	9.6

Diarrhea	Any	905	15	1.7	0.9	2.7	486	9	1.9	0.9	3.5
	Grade 3	905	6	0.7	0.2	1.4	486	6	1.2	0.5	2.7
	Related	905	6	0.7	0.2	1.4	486	8	1.6	0.7	3.2
Fever (axillary)	≥ 37.5 °C	905	244	27.0	24.1	30.0	486	142	29.2	25.2	33.5
	> 39.0 °C	905	2	0.2	0.0	0.8	486	4	0.8	0.2	2.1
	Related	905	164	18.1	15.7	20.8	486	95	19.5	16.1	23.4
Irritability/ Fussiness	Any	905	390	43.1	39.8	46.4	486	215	44.2	39.8	48.8
	Grade 3	905	21	2.3	1.4	3.5	486	7	1.4	0.6	2.9
	Related	905	238	26.3	23.5	29.3	486	123	25.3	21.5	29.4
Loss of appetite	Any	905	195	21.5	18.9	24.4	486	102	21.0	17.5	24.9
	Grade 3	905	6	0.7	0.2	1.4	486	1	0.2	0.0	1.1
	Related	905	118	13.0	10.9	15.4	486	57	11.7	9.0	14.9
Vomiting	Any	905	53	5.9	4.4	7.6	486	46	9.5	7.0	12.4
	Grade 3	905	9	1.0	0.5	1.9	486	7	1.4	0.6	2.9
	Related	905	18	2.0	1.2	3.1	486	23	4.7	3.0	7.0
Across doses											
Cough/ Runny nose	Any	914	366	40.0	36.8	43.3	490	205	41.8	37.4	46.3
	Grade 3	914	16	1.8	1.0	2.8	490	3	0.6	0.1	1.8
	Related	914	99	10.8	8.9	13.0	490	52	10.6	8.0	13.7
Diarrhea	Any	914	38	4.2	3.0	5.7	490	20	4.1	2.5	6.2
	Grade 3	914	9	1.0	0.5	1.9	490	10	2.0	1.0	3.7
	Related	914	24	2.6	1.7	3.9	490	15	3.1	1.7	5.0
Fever (axillary)	≥ 37.5 °C	914	310	33.9	30.8	37.1	490	192	39.2	34.8	43.7
	> 39.0 °C	914	2	0.2	0.0	0.8	490	4	0.8	0.2	2.1
	Related	914	234	25.6	22.8	28.6	490	137	28.0	24.0	32.2
Irritability/ Fussiness	Any	914	567	62.0	58.8	65.2	490	308	62.9	58.4	67.1
	Grade 3	914	40	4.4	3.1	5.9	490	25	5.1	3.3	7.4
	Related	914	395	43.2	40.0	46.5	490	218	44.5	40.0	49.0
Loss of appetite	Any	914	310	33.9	30.8	37.1	490	161	32.9	28.7	37.2
	Grade 3	914	9	1.0	0.5	1.9	490	2	0.4	0.0	1.5
	Related	914	202	22.1	19.4	24.9	490	107	21.8	18.3	25.8
Vomiting	Any	914	131	14.3	12.1	16.8	490	80	16.3	13.2	19.9
	Grade 3	914	18	2.0	1.2	3.1	490	12	2.4	1.3	4.2
	Related	914	56	6.1	4.7	7.9	490	40	8.2	5.9	11.0

N = number of subjects having received the considered dose of HRV vaccine/placebo
n (%) = number (percentage) of subjects with the specified symptom reported for the considered dose
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Any = any occurrence of the specified symptom, irrespective of intensity grade and relationship to vaccination
Grade 3 Cough/Runny nose = symptom that prevented normal activity
Grade 3 Irritability/Fussiness = crying that could not be comforted
Grade 3 Loss of appetite = not eating at all
Grade 3 Diarrhea = ≥ 6 looser than normal stools/day
Grade 3 Vomiting = ≥ 3 episodes of vomiting/day
Related = occurrence of the specified symptom was considered by the investigator as causally related to the vaccination

Safety Results: Number (%) of subjects with unsolicited adverse events (AEs) (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-30 following vaccination)	HRV Group N = 2646	Placebo Group N = 1348
Subjects with any AE(s), n (%)	1686 (63.7)	828 (61.4)
Pyrexia	612 (23.1)	316 (23.4)
Irritability	555 (21.0)	229 (17.0)
Rhinitis	308 (11.6)	163 (12.1)
Crying	219 (8.3)	111 (8.2)
Upper respiratory tract infection	193 (7.3)	94 (7.0)
Cough	136 (5.1)	76 (5.6)
Otitis media	126 (4.8)	69 (5.1)

Injection site pain	106 (4.0)	40 (3.0)
Flatulence	100 (3.8)	33 (2.4)
Conjunctivitis	85 (3.2)	41 (3.0)
Gastrointestinal disorder	77 (2.9)	37 (2.7)
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) (Total Vaccinated Cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	HRV Group N = 2646	Placebo Group N = 1348
Subjects with any SAE(s), n (%) [n related]	145 (5.5) [2]	95 (7.0) [0]
Bronchiolitis	18 (0.7) [0]	14 (1.0) [0]
Bronchitis	16 (0.6) [0]	9 (0.7) [0]
Gastroenteritis	9 (0.3) [1]	11 (0.8) [0]
Laryngitis	9 (0.3) [0]	6 (0.4) [0]
Pyelonephritis	9 (0.3) [0]	6 (0.4) [0]
Gastroenteritis rotavirus	0 (0.0) [0]	11 (0.8) [0]
Otitis media	9 (0.3) [0]	2 (0.1) [0]
Pyelonephritis acute	7 (0.3) [0]	4 (0.3) [0]
Pneumonia	7 (0.3) [0]	2 (0.1) [0]
Urinary tract infection	4 (0.2) [0]	4 (0.3) [0]
Bronchitis acute	5 (0.2) [0]	1 (0.1) [0]
Bronchopneumonia	5 (0.2) [0]	0 (0.0) [0]
Exanthema subitum	2 (0.1) [0]	3 (0.2) [0]
Pyrexia	3 (0.1) [0]	2 (0.1) [0]
Respiratory tract infection	3 (0.1) [0]	2 (0.1) [0]
Concussion	2 (0.1) [0]	2 (0.1) [0]
Asthma	1 (0.0) [0]	2 (0.1) [0]
Convulsion	1 (0.0) [0]	2 (0.1) [0]
Enterocolitis	2 (0.1) [0]	1 (0.1) [0]
Febrile convulsion	2 (0.1) [0]	1 (0.1) [0]
Inguinal hernia	2 (0.1) [0]	1 (0.1) [0]
Upper respiratory tract infection	2 (0.1) [0]	1 (0.1) [0]
Viral infection	2 (0.1) [0]	1 (0.1) [0]
Cellulitis	1 (0.0) [0]	1 (0.1) [0]
Contusion	1 (0.0) [0]	1 (0.1) [0]
Diarrhea	1 (0.0) [0]	1 (0.1) [0]
Ear infection	0 (0.0) [0]	2 (0.1) [0]
Epilepsy	0 (0.0) [0]	2 (0.1) [0]
Nasopharyngitis	1 (0.0) [0]	1 (0.1) [0]
Pneumonia respiratory syncytial viral	1 (0.0) [0]	1 (0.1) [0]
Respiratory syncytial virus infection	2 (0.1) [0]	0 (0.0) [0]
Testicular torsion	0 (0.0) [0]	2 (0.1) [0]
Thermal burn	1 (0.0) [0]	1 (0.1) [0]
Vomiting	2 (0.1) [0]	0 (0.0) [0]
Adenoidal hypertrophy	1 (0.0) [0]	0 (0.0) [0]
Animal bite	0 (0.0) [0]	1 (0.1) [0]
Apnea	0 (0.0) [0]	1 (0.1) [0]
Aspiration	1 (0.0) [0]	0 (0.0) [0]
Atrioventricular septal defect	1 (0.0) [0]	0 (0.0) [0]
Bacterial pyelonephritis	1 (0.0) [0]	0 (0.0) [0]
Balance disorder	1 (0.0) [0]	0 (0.0) [0]
Breath holding	1 (0.0) [0]	0 (0.0) [0]
Bronchospasm	1 (0.0) [0]	0 (0.0) [0]
Clavicle fracture	1 (0.0) [0]	0 (0.0) [0]
Conjunctivitis	1 (0.0) [0]	0 (0.0) [0]
Constipation	1 (0.0) [0]	0 (0.0) [0]

Cow's milk intolerance	1 (0.0) [0]	0 (0.0) [0]
Coxsackie viral infection	1 (0.0) [0]	0 (0.0) [0]
Dermatitis atopic	1 (0.0) [0]	0 (0.0) [0]
Dyspnea	1 (0.0) [0]	0 (0.0) [0]
Escherichia urinary tract infection	0 (0.0) [0]	1 (0.1) [0]
Fall	0 (0.0) [0]	1 (0.1) [0]
Femur fracture	1 (0.0) [0]	0 (0.0) [0]
Foreign body trauma	1 (0.0) [0]	0 (0.0) [0]
Gastroenteritis adenovirus	1 (0.0) [0]	0 (0.0) [0]
Gastroenteritis bacterial	0 (0.0) [0]	1 (0.1) [0]
Gastroenteritis salmonella	1 (0.0) [0]	0 (0.0) [0]
Gastrointestinal disorder	1 (0.0) [0]	0 (0.0) [0]
Gastro esophageal reflux disease	1 (0.0) [0]	0 (0.0) [0]
Hematuria	1 (0.0) [0]	0 (0.0) [0]
Herpetic gingivostomatitis	0 (0.0) [0]	1 (0.1) [0]
Hypoglycemia	1 (0.0) [0]	0 (0.0) [0]
Hypotonia	1 (0.0) [0]	0 (0.0) [0]
Infantile spasms	0 (0.0) [0]	1 (0.1) [0]
Infection	0 (0.0) [0]	1 (0.1) [0]
Intussusception*	1 (0.0) [1]	0 (0.0) [0]
Lissencephaly	0 (0.0) [0]	1 (0.1) [0]
Lobar pneumonia	0 (0.0) [0]	1 (0.1) [0]
Loss of consciousness	0 (0.0) [0]	1 (0.1) [0]
Medical observation	1 (0.0) [0]	0 (0.0) [0]
Meningitis	1 (0.0) [0]	0 (0.0) [0]
Milk allergy	0 (0.0) [0]	1 (0.1) [0]
Orchitis	1 (0.0) [0]	0 (0.0) [0]
Otitis media acute	1 (0.0) [0]	0 (0.0) [0]
Perianal abscess	1 (0.0) [0]	0 (0.0) [0]
Pertussis	1 (0.0) [0]	0 (0.0) [0]
Pneumonia viral	1 (0.0) [0]	0 (0.0) [0]
Scrotal edema	1 (0.0) [0]	0 (0.0) [0]
Sepsis	1 (0.0) [0]	0 (0.0) [0]
Sleep disorder	1 (0.0) [0]	0 (0.0) [0]
Subcutaneous abscess	1 (0.0) [0]	0 (0.0) [0]
Syncope	0 (0.0) [0]	1 (0.1) [0]
Testicular cyst	1 (0.0) [0]	0 (0.0) [0]
Tibia fracture	1 (0.0) [0]	0 (0.0) [0]
Varicella	1 (0.0) [0]	0 (0.0) [0]
* One case of intussusception, assessed as related to vaccination, was reported 8 days after Dose 2 of HRV vaccine; the subject recovered completely.		
Fatal SAEs	HRV Group N = 2646	Placebo Group N = 1348
Subjects with fatal SAEs, n (%) [related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
Please refer to the publications section.

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