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.: 107876 (Rota-061)

Title: A phase III, randomised study to evaluate the clinical consistency in terms of immunogenicity and reactogenicity of three production lots of the liquid formulation of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine and to evaluate the liquid formulation as compared to the lyophilised formulation of the HRV vaccine in terms of immunogenicity, reactogenicity and safety when administered as a two-dose primary vaccination in healthy infants previously uninfected with human rotavirus.
Rotarix: GSK Biologicals' HRV vaccine

Rationale: The aim of this study was to evaluate the lot-to-lot consistency of three consecutive production lots of the HRV vaccine liquid formulation in terms of immunogenicity and safety. This study also evaluated the immunogenicity and safety of the liquid formulation compared to the lyophilised formulation of the HRV vaccine when administered concomitantly with routine childhood vaccine (Infanrix Hexa).
Infanrix Hexa (DTPa-HBV-IPV/Hib): GSK Biologicals' combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliovirus and *Haemophilus influenzae* type b vaccine.

Phase: III

Study Period: 10 November 2006 to 13 September 2007

Study Design: Multi-centric, randomised (1:1:1:1) study with 4 parallel treatment groups. The study was double blind for the 3 lots of HRV vaccine liquid formulation, and open label for liquid versus the lyophilised formulation.

Centres: 12 study centres in Finland

Indication: Two-dose immunisation at 3 and 4 months of age in healthy infants previously uninfected with human rotavirus.

Treatment: The study groups were as follows:

- Liq_A Group: subjects received 2 doses of HRV vaccine liquid formulation Lot A
- Liq_B Group: subjects received 2 doses of HRV vaccine liquid formulation Lot B
- Liq_C Group: subjects received 2 doses of HRV vaccine liquid formulation Lot C
- Lyo Group: subjects received 2 doses of HRV vaccine lyophilised formulation

Subjects received one dose of HRV vaccine (liquid formulation or lyophilised formulation) each at Visit 1 and Visit 2 (at approximately 3 and 4 months of age, respectively) orally. The first 2 doses of DTPa-HBV-IPV/Hib vaccine were co-administered with each dose of the HRV vaccine.
Note: Visits 1, 2 and 3 corresponded to Months 0, 1 and 2 in the schedule.
For some of the analyses, the 3 groups receiving the different HRV vaccine liquid formulation production lots were pooled into Liq Pool Group.

Objectives:

- To demonstrate the lot-to-lot consistency of the liquid formulation of HRV vaccine in terms of immunogenicity as measured by serum anti-rotavirus (RV) Immunoglobulin A (IgA) antibody levels one month after Dose 2.

Criterion to reach this objective: Consistency would be reached if, for all pairs of lots, the two-sided 95% confidence intervals (CIs) for the ratio of anti-RV IgA antibody GMCs one month after Dose 2 were within the [0.5; 2] clinical limit interval.

- To demonstrate non-inferiority of the liquid formulation of HRV vaccine to that of lyophilised formulation of HRV vaccine in terms of seroconversion rates one month after Dose 2.

Criterion to reach this objective: Non-inferiority would be reached if the upper limit of the two-sided asymptotic standardised 95% CI for the difference in seroconversion rate between the lyophilised formulation of HRV vaccine and (minus) the liquid formulation of HRV vaccine was less than or equal to 10%.

Primary Outcome/Efficacy Variable:

- Serum anti-RV IgA antibody concentration at Visit 3 in each HRV vaccine liquid formulation group.
- Seroconversion to anti-RV IgA antibody at Visit 3.

Seroconversion was defined as appearance of anti-RV IgA antibody concentration $\geq$ 20 U/mL in subjects initially (i.e. prior to the first dose of HRV vaccine) seronegative (i.e. with anti-RV IgA antibody concentration < 20 U/mL).

Secondary Outcome/Efficacy Variable(s):

Immunogenicity

- Serum anti-RV IgA antibody concentration at Visit 3 in the HRV vaccine lyophilised formulation group.

Safety

- Occurrence of each type of solicited symptom within the 8-day solicited follow-up period (Day 0-7) after each dose of HRV vaccine.
- Occurrence of unsolicited adverse events (AEs) within 31 days (Day 0-30) after any dose of HRV vaccine, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence of serious adverse events (SAEs) from Dose 1 of HRV vaccine up to 6 months after the last dose of HRV vaccine.
- Presence of RV in Gastroenteritis (GE) stools collected from Dose 1 of HRV vaccine up to Visit 3.

Statistical Methods:

The analyses were performed on the According-To-Protocol (ATP) cohort for immunogenicity and the Total vaccinated cohort.

The ATP cohort for immunogenicity included all subjects:

- who had received at least one dose of study vaccine,
- who had not received a replacement vial, except if the appropriate vaccine was administered in "double-blind replacement",
- for whom the randomisation code had not been broken,
- for whom the HRV vaccine liquid or lyophilised formulation was administered according to protocol,
- who had not received a vaccine forbidden by or not specified in the protocol,
- who were seronegative for serum anti-RV IgA antibodies on the day of Dose 1,
- 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 liquid or lyophilised formulation,
- who complied with blood sampling schedule,
- for whom immunogenicity data were available at post-sampling time point,
- who had no RV other than vaccine strain in GE stool samples collected up to Visit 3,
- who had no concomitant infection unrelated to the vaccine which could have influenced the immune responses.

The Total vaccinated cohort included all subjects with at least one study vaccine administration documented.

Analysis of immunogenicity:

The analysis was performed on the ATP cohort for immunogenicity.

Descriptive analysis

For each study group, at each time point that anti-RV IgA antibody concentrations were measured, seropositivity/ seroconversion rates with their exact 95% CI and geometric mean concentrations (GMCs) with their 95% CI were tabulated.

Inferential analysis

The 3 lots of the HRV vaccine liquid formulation were considered consistent at Visit 3, if for each pair of lots, the two-sided 95% CIs for the ratio of anti-RV IgA antibody GMCs 1 month after Dose 2 of HRV vaccine were within the [0.5; 2] clinical limit interval.

Non-inferiority, in terms of seroconversion rates at Visit 3, of the HRV vaccine liquid formulation to the lyophilised formulation was demonstrated if the upper limit of the two-sided asymptotic standardised 95% CI for the difference in seroconversion rate at one month after Dose 2 of HRV vaccine between the HRV vaccine lyophilised formulation group and (minus) the pooled HRV vaccine liquid formulation group was less than or equal to 10%.

Analysis of safety:

The analysis was performed on the Total vaccinated cohort.

For each group, the percentage of subjects with each individual solicited general symptom over the 8-day solicited follow-up period (Day 0-7) was computed, along with exact 95% CI. The same calculations were done for each individual general solicited symptom rated as grade 3 in intensity and for each individual solicited general symptom assessed as related to vaccination.

The percentage of subjects with the presence of RV in GE stools collected from Dose 1 of HRV vaccine up to Visit 3 was tabulated.

The percentage of subjects with unsolicited AEs reported during the 31-day follow-up period (Day 0-30) after each vaccination was tabulated per group, according to the MedDRA preferred terms.

The occurrence of SAEs from Dose 1 of HRV vaccine up to 6 months after the last dose of HRV vaccine was tabulated per group, according to the MedDRA preferred terms.

Study Population: Male or female infants between, and including, 10-17 weeks (70-125 days) of age at the time of the first study vaccination with birth weight > 2000g, free of obvious health problems as established by medical history and clinical examination before entering into the study and for whom the investigator believed that their parents/guardians

would comply with the requirements of the protocol. Written informed consent was obtained from the parents/guardians of each subject.

Number of subjects	Liq_A Group	Liq_B Group	Liq_C Group	Liq_Pool Group	Lyo Group
Planned, N	300	300	300	900	300
Randomised, N (Total vaccinated cohort)	298	302	300	900	300
Completed, n (%)	297 (99.7)	301 (99.7)	298 (99.3)	896 (99.6)	297 (99.0)
Total Number Subjects Withdrawn, n (%)	1 (0.3)	1 (0.3)	2 (0.7)	4 (0.4)	3 (1.0)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	1 (0.3)	1 (0.3)	2 (0.7)	4 (0.4)	2 (0.7)
Demographics	Liq_A Group	Liq_B Group	Liq_C Group	Liq_Pool Group	Lyo Group
N (Total vaccinated cohort)	298	302	300	900	300
Females:Males	160:138	146:156	150:150	456:444	138:162
Mean Age, weeks (SD)	11.6 (1.32)	11.6 (1.22)	11.5 (1.27)	11.6 (1.27)	11.6 (1.17)
White/Caucasian, n (%)	295 (99.0)	299 (99.0)	296 (98.7)	890 (98.9)	295 (98.3)

Primary Efficacy Results:
Ratio of anti-rotavirus IgA antibody GMCs at one month after Dose 2 of the HRV vaccine between each pair of the 3 lots of the HRV vaccine liquid formulation (ATP cohort for immunogenicity)

Group	N	GMC (U/mL)	Group	N	GMC (U/mL)	GMC ratio			
						Ratio order	Value	95% CI	
								LL	UL
Liq_A	242	384.4	Liq_B	260	418.8	Liq_A /Liq_B	0.92	0.67*	1.26*
Liq_A	242	384.4	Liq_C	244	324.4	Liq_A /Liq_C	1.19	0.86*	1.64*
Liq_B	260	418.8	Liq_C	244	324.4	Liq_B /Liq_C	1.29	0.94*	1.77*

N = number of subjects with available results
95% CI = 95% Confidence Interval (one-way ANOVA model with pooled variance from the four groups)
LL = Lower Limit, UL = Upper Limit
*Lot-to-Lot consistency objective was reached as the two-sided 95% CIs were within [0.5; 2]

Primary Efficacy Results:
Difference between lyophilised formulation group and the pooled HRV vaccine liquid formulation group in the percentage of subjects who seroconverted for the serum anti-rotavirus IgA antibody at one month after Dose 2 of the HRV vaccine (ATP cohort for immunogenicity)

Group	N	%	Group	N	%	Difference in seroconversion rate			
						Difference	%	95% CI	
								LL	UL
Liq_Pool	746	88.6	Lyo	252	90.5	Lyo - Liq_Pool	1.87	-2.85	5.83*

N = number of subjects with available results
% = percentage of subjects who seroconverted at Visit 3
95% CI = asymptotic standardised 95% Confidence Interval; LL = Lower Limit; UL = Upper Limit
*Non-inferiority objective was reached as the upper limit of the 95% CI ≤ 10%

Primary Efficacy Results:
Anti-rotavirus IgA antibody seroconversion rates and GMC, calculated on all subjects (ATP cohort for immunogenicity)

Group	Timing	N	≥ 20 U/mL				GMC (U/mL)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Liq_A	Pre	242	0	0.0	0.0	1.5	< 20	-	-
	PII(M2)*	242	220	90.9	86.6	94.2	384.4	309.1	478.2
Liq_B	Pre	260	0	0.0	0.0	1.4	< 20	-	-
	PII(M2)*	260	235	90.4	86.1	93.7	418.8	337.8	519.1
Liq_C	Pre	244	0	0.0	0.0	1.5	<20	-	-
	PII(M2)*	244	206	84.4	79.3	88.7	324.4	253.4	415.3
Liq_Pool	Pre	746	0	0.0	0.0	0.5	< 20	-	-
	PII(M2)*	746	661	88.6	86.1	90.8	374.7	328.8	426.9
Lyo	Pre	252	0	0.0	0.0	1.5	< 20	-	-
	PII(M2)*	252	228	90.5	86.2	93.8	331.8	265.0	415.4

N = number of subjects with available results
n (%) = number (percentage) of subjects with antibody concentration above the cut-off
95% CI = 95% Confidence Interval; LL = Lower Limit; UL = Upper Limit
Pre = pre-vaccination
PII (M2) = blood sample taken one month after Dose 2 of HRV vaccine (Visit 3)
* Primary Efficacy Results

Secondary Outcome Variable (s):
Percentage of subjects with each solicited general symptom including those rated grade 3 in intensity and those assessed as related to vaccination during the 8-day (Day 0-7) follow-up period, for each dose in each HRV vaccine liquid formulation group (Total vaccinated cohort)

Symptom	Intensity/ relationship	Liq_A Group				Liq_B Group				Liq_C Group			
		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL
		Dose 1											
		N = 298				N = 302				N = 300			
Cough/ runny nose	Any	72	24.2	19.4	29.4	90	29.8	24.7	35.3	71	23.7	19.0	28.9
	Grade 3	1	0.3	0.0	1.9	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Related	62	20.8	16.3	25.9	76	25.2	20.4	30.5	49	16.3	12.3	21.0
Diarrhoea	Any	8	2.7	1.2	5.2	9	3.0	1.4	5.6	8	2.7	1.2	5.2
	Grade 3	3	1.0	0.2	2.9	2	0.7	0.1	2.4	2	0.7	0.1	2.4
	Related	8	2.7	1.2	5.2	9	3.0	1.4	5.6	8	2.7	1.2	5.2
Fever (rectal)	≥ 38.0°C	63	21.1	16.6	26.2	59	19.5	15.2	24.5	57	19.0	14.7	23.9
	> 39.5°C	1	0.3	0.0	1.9	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Related	61	20.5	16.0	25.5	58	19.2	14.9	24.1	55	18.3	14.1	23.2
Irritability	Any	213	71.5	66.0	76.5	225	74.5	69.2	79.3	191	63.7	57.9	69.1
	Grade 3	12	4.0	2.1	6.9	17	5.6	3.3	8.9	9	3.0	1.4	5.6
	Related	203	68.1	62.5	73.4	220	72.8	67.5	77.8	184	61.3	55.6	66.9
Loss of appetite	Any	79	26.5	21.6	31.9	79	26.2	21.3	31.5	73	24.3	19.6	29.6
	Grade 3	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Related	75	25.2	20.3	30.5	78	25.8	21.0	31.2	67	22.3	17.7	27.5
Vomiting	Any	47	15.8	11.8	20.4	45	14.9	11.1	19.4	44	14.7	10.9	19.2
	Grade 3	11	3.7	1.9	6.5	7	2.3	0.9	4.7	7	2.3	0.9	4.7
	Related	45	15.1	11.2	19.7	43	14.2	10.5	18.7	39	13.0	9.4	17.3
		Dose 2											
		N = 297				N = 301				N = 300			
Cough/ runny nose	Any	92	31.0	25.8	36.6	104	34.6	29.2	40.2	95	31.7	26.4	37.3
	Grade 3	2	0.7	0.1	2.4	2	0.7	0.1	2.4	4	1.3	0.4	3.4
	Related	79	26.6	21.7	32.0	84	27.9	22.9	33.3	79	26.3	21.4	31.7
Diarrhoea	Any	3	1.0	0.2	2.9	7	2.3	0.9	4.7	12	4.0	2.1	6.9
	Grade 3	1	0.3	0.0	1.9	2	0.7	0.1	2.4	2	0.7	0.1	2.4
	Related	3	1.0	0.2	2.9	7	2.3	0.9	4.7	12	4.0	2.1	6.9
Fever (rectal)	≥ 38.0°C	80	26.9	22.0	32.4	79	26.2	21.4	31.6	94	31.3	26.1	36.9
	> 39.5°C	2	0.7	0.1	2.4	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Related	79	26.6	21.7	32.0	76	25.2	20.4	30.6	91	30.3	25.2	35.9
Irritability	Any	201	67.7	62.0	73.0	224	74.4	69.1	79.3	202	67.3	61.7	72.6
	Grade 3	11	3.7	1.9	6.5	18	6.0	3.6	9.3	14	4.7	2.6	7.7
	Related	195	65.7	60.0	71.0	220	73.1	67.7	78.0	200	66.7	61.0	72.0
Loss of appetite	Any	69	23.2	18.5	28.5	63	20.9	16.5	26.0	70	23.3	18.7	28.5
	Grade 3	1	0.3	0.0	1.9	0	0.0	0.0	1.2	0	0.0	0.0	1.2
	Related	67	22.6	17.9	27.7	59	19.6	15.3	24.5	68	22.7	18.1	27.8
Vomiting	Any	43	14.5	10.7	19.0	40	13.3	9.7	17.7	33	11.0	7.7	15.1
	Grade 3	7	2.4	1.0	4.8	8	2.7	1.2	5.2	8	2.7	1.2	5.2
	Related	40	13.5	9.8	17.9	40	13.3	9.7	17.7	32	10.7	7.4	14.7
		Across doses											
		N = 298				N = 302				N = 300			

Cough/ runny nose	Any	134	45.0	39.2	50.8	147	48.7	42.9	54.5	132	44.0	38.3	49.8
	Grade 3	3	1.0	0.2	2.9	2	0.7	0.1	2.4	5	1.7	0.5	3.8
	Related	118	39.6	34.0	45.4	125	41.4	35.8	47.2	108	36.0	30.6	41.7
Diarrhoea	Any	11	3.7	1.9	6.5	15	5.0	2.8	8.1	19	6.3	3.9	9.7
	Grade 3	4	1.3	0.4	3.4	4	1.3	0.4	3.4	3	1.0	0.2	2.9
	Related	11	3.7	1.9	6.5	15	5.0	2.8	8.1	19	6.3	3.9	9.7
Fever (rectal)	≥ 38.0°C	111	37.2	31.7	43.0	104	34.4	29.1	40.1	122	40.7	35.1	46.5
	> 39.5°C	3	1.0	0.2	2.9	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Related	109	36.6	31.1	42.3	100	33.1	27.8	38.7	118	39.3	33.8	45.1
Irritability	Any	254	85.2	80.7	89.1	267	88.4	84.3	91.8	240	80.0	75.0	84.4
	Grade 3	20	6.7	4.1	10.2	31	10.3	7.1	14.3	21	7.0	4.4	10.5
	Related	252	84.6	80.0	88.5	265	87.7	83.5	91.2	238	79.3	74.3	83.8
Loss of appetite	Any	111	37.2	31.7	43.0	113	37.4	31.9	43.1	111	37.0	31.5	42.7
	Grade 3	1	0.3	0.0	1.9	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Related	106	35.6	30.1	41.3	108	35.8	30.4	41.5	109	36.3	30.9	42.1
Vomiting	Any	70	23.5	18.8	28.7	59	19.5	15.2	24.5	61	20.3	15.9	25.3
	Grade 3	18	6.0	3.6	9.4	12	4.0	2.1	6.8	12	4.0	2.1	6.9
	Related	69	23.2	18.5	28.4	58	19.2	14.9	24.1	58	19.3	15.0	24.3
		Liq_Pool Group						Lyo Group					
				95 % CI						95 % CI			
		n	%	LL	UL			n	%	LL	UL		
		Dose 1											
		N = 900						N = 300					
Cough/ runny nose	Any	233	25.9	23.1	28.9			79	26.3	21.4	31.7		
	Grade 3	2	0.2	0.0	0.8			4	1.3	0.4	3.4		
	Related	187	20.8	18.2	23.6			64	21.3	16.8	26.4		
Diarrhoea	Any	25	2.8	1.8	4.1			4	1.3	0.4	3.4		
	Grade 3	7	0.8	0.3	1.6			1	0.3	0.0	1.8		
	Related	25	2.8	1.8	4.1			3	1.0	0.2	2.9		
Fever (rectal)	≥ 38.0°C	179	19.9	17.3	22.6			68	22.7	18.1	27.8		
	> 39.5°C	2	0.2	0.0	0.8			0	0.0	0.0	1.2		
	Related	174	19.3	16.8	22.1			67	22.3	17.7	27.5		
Irritability	Any	629	69.9	66.8	72.9			207	69.0	63.4	74.2		
	Grade 3	38	4.2	3.0	5.7			12	4.0	2.1	6.9		
	Related	607	67.4	64.3	70.5			201	67.0	61.4	72.3		
Loss of appetite	Any	231	25.7	22.8	28.7			67	22.3	17.7	27.5		
	Grade 3	1	0.1	0.0	0.6			1	0.3	0.0	1.8		
	Related	220	24.4	21.7	27.4			63	21.0	16.5	26.1		
Vomiting	Any	136	15.1	12.8	17.6			55	18.3	14.1	23.2		
	Grade 3	25	2.8	1.8	4.1			11	3.7	1.8	6.5		
	Related	127	14.1	11.9	16.6			51	17.0	12.9	21.7		
		Dose 2											
		N = 898						N = 299					
Cough/ runny nose	Any	291	32.4	29.4	35.6			109	36.5	31.0	42.2		
	Grade 3	8	0.9	0.4	1.7			2	0.7	0.1	2.4		
	Related	242	26.9	24.1	30.0			89	29.8	24.6	35.3		
Diarrhoea	Any	22	2.4	1.5	3.7			8	2.7	1.2	5.2		
	Grade 3	5	0.6	0.2	1.3			3	1.0	0.2	2.9		
	Related	22	2.4	1.5	3.7			8	2.7	1.2	5.2		
Fever (rectal)	≥ 38.0°C	253	28.2	25.3	31.2			74	24.7	20.0	30.0		
	> 39.5°C	4	0.4	0.1	1.1			3	1.0	0.2	2.9		
	Related	246	27.4	24.5	30.4			71	23.7	19.0	29.0		
Irritability	Any	627	69.8	66.7	72.8			200	66.9	61.2	72.2		
	Grade 3	43	4.8	3.5	6.4			12	4.0	2.1	6.9		
	Related	615	68.5	65.3	71.5			196	65.6	59.9	70.9		

Loss of appetite	Any	202	22.5	19.8	25.4	62	20.7	16.3	25.8
	Grade 3	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Related	194	21.6	19.0	24.4	60	20.1	15.7	25.1
Vomiting	Any	116	12.9	10.8	15.3	41	13.7	10.0	18.1
	Grade 3	23	2.6	1.6	3.8	11	3.7	1.9	6.5
	Related	112	12.5	10.4	14.8	40	13.4	9.7	17.8
		Across doses							
		N = 900				N = 300			
Cough/ runny nose	Any	413	45.9	42.6	49.2	149	49.7	43.9	55.5
	Grade 3	10	1.1	0.5	2.0	6	2.0	0.7	4.3
	Related	351	39.0	35.8	42.3	127	42.3	36.7	48.1
Diarrhoea	Any	45	5.0	3.7	6.6	11	3.7	1.8	6.5
	Grade 3	11	1.2	0.6	2.2	4	1.3	0.4	3.4
	Related	45	5.0	3.7	6.6	10	3.3	1.6	6.0
Fever (rectal)	≥ 38.0°C	337	37.4	34.3	40.7	110	36.7	31.2	42.4
	> 39.5°C	6	0.7	0.2	1.4	3	1.0	0.2	2.9
	Related	327	36.3	33.2	39.6	107	35.7	30.2	41.4
Irritability	Any	761	84.6	82.0	86.9	249	83.0	78.3	87.1
	Grade 3	72	8.0	6.3	10.0	22	7.3	4.7	10.9
	Related	755	83.9	81.3	86.2	247	82.3	77.5	86.5
Loss of appetite	Any	335	37.2	34.1	40.5	101	33.7	28.3	39.3
	Grade 3	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Related	323	35.9	32.8	39.1	96	32.0	26.8	37.6
Vomiting	Any	190	21.1	18.5	23.9	73	24.3	19.6	29.6
	Grade 3	42	4.7	3.4	6.3	17	5.7	3.3	8.9
	Related	185	20.6	18.0	23.3	68	22.7	18.1	27.8

N = number of subjects having received the considered dose
n (%) = number (percentage) of subjects for whom the specified symptom was reported for the considered dose
Any = any occurrence of the specified symptom, irrespective of intensity grade and relationship to vaccination
Grade 3 Cough/runny nose = cough/runny nose which prevented daily activity
Grade 3 Diarrhoea = ≥ 6 looser than normal stools/day
Grade 3 Irritability = crying that could not be comforted/ prevented normal activity
Grade 3 Loss of appetite = not eating at all
Grade 3 Vomiting = ≥ 3 episodes of vomiting/day
Related = any occurrence of the specified symptom assessed as causally related to the vaccination

Secondary Outcome Variable (s):
Percentage of subjects reporting RV (vaccine strain or wild type RV) GE episodes from Dose 1 of HRV vaccine up to Visit 3 (Total vaccinated cohort)

Group	Between Dose 1 and before Dose 2					Between Dose 2 and Visit 3					Between Dose 1 and Visit 3				
	N	n	%	95% CI		N	n	%	95% CI		N	n	%	95% CI	
				LL	UL				LL	UL				LL	UL
Liq_A	298	0	0.0	0.0	1.2	297	0	0.0	0.0	1.2	298	0	0.0	0.0	1.2
Liq_B	302	1	0.3	0.0	1.8	301	0	0.0	0.0	1.2	302	1	0.3	0.0	1.8
Liq_C	300	0	0.0	0.0	1.2	300	1	0.3	0.0	1.8	300	1	0.3	0.0	1.8
Liq_Pool	900	1	0.1	0.0	0.6	898	1	0.1	0.0	0.6	900	2	0.2	0.0	0.8
Lyo	300	0	0.0	0.0	1.2	299	0	0.0	0.0	1.2	300	0	0.0	0.0	1.2

Between Dose 1 and before Dose 2: N = number of subjects having received the first dose
Between Dose 2 and Visit 3: N = number of subjects having received the second dose
Between Dose 1 and Visit 3: N = number of subjects having received at least one dose
n (%) = number (percentage) of subjects reporting at least one RV GE episode during the specified period
95% CI = exact 95% Confidence Interval, LL = Lower Limit, UL = Upper Limit

Safety Results: Number (%) of subjects with unsolicited adverse events (Total vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-30 following vaccination)	Liq_A Group N = 298	Liq_B Group N = 302	Liq_C Group N = 300	Liq_Pool Group N = 900	Lyo Group N = 300
Subjects with any AE(s), n (%)	142 (47.7)	145 (48.0)	142 (47.3)	429 (47.7)	159 (53.0)

Upper respiratory tract infection	20 (6.7)	25 (8.3)	24 (8.0)	69 (7.7)	26 (8.7)
Rhinitis	24 (8.1)	22 (7.3)	19 (6.3)	65 (7.2)	23 (7.7)
Flatulence	16 (5.4)	16 (5.3)	14 (4.7)	46 (5.1)	20 (6.7)
Pyrexia	16 (5.4)	14 (4.6)	20 (6.7)	50 (5.6)	12 (4.0)
Somnolence	15 (5.0)	18 (6.0)	14 (4.7)	47 (5.2)	18 (6.0)
Otitis media	8 (2.7)	15 (5.0)	19 (6.3)	42 (4.7)	18 (6.0)
Cough	11 (3.7)	11 (3.6)	16 (5.3)	38 (4.2)	12 (4.0)
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) up to the safety follow-up conclusion (Total vaccinated cohort)					
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]					
All SAEs	Liq_A Group N = 298	Liq_B Group N = 302	Liq_C Group N = 300	Liq_Pool Group N = 900	Lyo Group N = 300
Subjects with any SAE(s), n (%) [n related]	5 (1.7) [0]	9 (3.0) [0]	14 (4.7) [0]	28 (3.1) [0]	8 (2.7) [0]
Gastroenteritis	0 (0.0) [0]	0 (0.0) [0]	3 (1.0) [0]	3 (0.3) [0]	1 (0.3) [0]
Laryngitis	1 (0.3) [0]	1 (0.3) [0]	1 (0.3) [0]	3 (0.3) [0]	1 (0.3) [0]
Otitis media	1 (0.3) [0]	2 (0.7) [0]	0 (0.0) [0]	3 (0.3) [0]	1 (0.3) [0]
Bronchial obstruction	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]	1 (0.1) [0]	1 (0.3) [0]
Bronchiolitis	0 (0.0) [0]	2 (0.7) [0]	0 (0.0) [0]	2 (0.2) [0]	0 (0.0) [0]
Convulsion	0 (0.0) [0]	0 (0.0) [0]	2 (0.7) [0]	2 (0.2) [0]	0 (0.0) [0]
Pneumonia	1 (0.3) [0]	1 (0.3) [0]	0 (0.0) [0]	2 (0.2) [0]	0 (0.0) [0]
Pyelonephritis	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]	1 (0.1) [0]	1 (0.3) [0]
Respiratory syncytial virus bronchiolitis	0 (0.0) [0]	0 (0.0) [0]	2 (0.7) [0]	2 (0.2) [0]	0 (0.0) [0]
Respiratory syncytial virus infection	1 (0.3) [0]	0 (0.0) [0]	1 (0.3) [0]	2 (0.2) [0]	0 (0.0) [0]
Bronchitis	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]
Dacryocystitis	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]	1 (0.1) [0]	0 (0.0) [0]
Febrile convulsion	1 (0.3) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Infantile spasms	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]
Influenza	0 (0.0) [0]	1 (0.3) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Inguinal hernia	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]	1 (0.1) [0]	0 (0.0) [0]
Kawasaki's disease	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [1]*
Lymphadenitis	0 (0.0) [0]	1 (0.3) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Pharyngitis	1 (0.3) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Pneumonia viral	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]
Pyelonephritis acute	0 (0.0) [0]	1 (0.3) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Upper respiratory tract infection	0 (0.0) [0]	1 (0.3) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Urinary tract infection	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]	1 (0.1) [0]	0 (0.0) [0]
Fatal SAEs	Liq_A Group N = 298	Liq_B Group N = 302	Liq_C Group N = 300	Liq_Pool Group N = 900	Lyo Group N = 300
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
*Following a few reports of the association of Kawasaki disease with other rotavirus vaccine, the principal investigator retrospectively concluded that Kawasaki disease was possibly related to vaccination.					

Conclusion: One month after Dose 2, 88.6% of the subjects of the Liq_Pool Group and 90.5% of the subjects of the Lyo Group had anti-rotavirus IgA antibody concentrations $\geq$ 20 U/mL. Irritability was the most frequently reported solicited general symptom. At least one unsolicited AE was reported for 429 (47.7%) and 159 (53.0%) subjects in the Liq_Pool Group and Lyo Group, respectively. From Dose 1 up to 6 months after the last dose of HRV vaccine, SAEs were reported for 28 (3.1%) and 8 (2.7%) subjects in the Liq_Pool Group and Lyo Group, respectively: one of the SAEs reported in the Lyo Group was considered by the investigator as related to the study vaccination. No fatal SAEs were reported.
Please refer also to the publication citations.

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