



Clinical trial results:

A phase IIIA, randomised, observer-blind, multi-centre study to evaluate the clinical consistency of three production lots of the Porcine circovirus (PCV)-free liquid formulation of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine and to evaluate the PCV-free liquid formulation of GSK Biologicals' HRV vaccine as compared to the currently licensed lyophilised formulation of the HRV vaccine in terms of immunogenicity, reactogenicity and safety when administered as a two-dose vaccination in healthy infants starting at age 6-12 weeks.

Summary

EudraCT number	2016-000598-19
Trial protocol	FI DE Outside EU/EEA ES
Global end of trial date	26 November 2018

Results information

Result version number	v1 (current)
This version publication date	07 June 2019
First version publication date	07 June 2019

Trial information

Trial identification

Sponsor protocol code	115461
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02914184
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 February 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The three co-primary objectives of the study were to demonstrate the lot-to-lot consistency of the PCV-free liquid HRV vaccine in terms of immunogenicity as measured by serum anti-RV IgA antibody concentrations 1-2 months after Dose 2, to demonstrate the immunological non-inferiority of PCV-free liquid HRV vaccine as compared to the currently licensed lyophilized HRV vaccine in terms of seroconversion rates 1-2 months after Dose 2 and to demonstrate the non-inferiority of the PCV-free liquid HRV vaccine to that of the currently licensed lyophilized HRV vaccine in terms of serum anti-RV IgA antibody concentrations 1-2 months after Dose 2.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of the vaccines, with appropriate medical treatment readily available in case of anaphylaxis. The Independent Data Monitoring Committee (IDMC) periodically reviewed safety data and made a recommendation on study continuation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Costa Rica: 90
Country: Number of subjects enrolled	Finland: 117
Country: Number of subjects enrolled	Germany: 71
Country: Number of subjects enrolled	Japan: 160
Country: Number of subjects enrolled	Korea, Republic of: 60
Country: Number of subjects enrolled	Spain: 501
Country: Number of subjects enrolled	Taiwan: 150
Country: Number of subjects enrolled	United States: 451
Worldwide total number of subjects	1600
EEA total number of subjects	689

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1600
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 66 centers in 8 countries: 2 in Costa Rica, 10 in Finland, 6 in Germany, 7 in Japan, 6 in Republic of Korea, 9 in Spain, 6 in Taiwan and 20 in the United States (US).

Pre-assignment

Screening details:

Among 1612 subjects enrolled in the study, 1600 were vaccinated and 1545 completed the study.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Observer-blind (double blind for the 3 lots of PCV-free HRV liquid vaccine and observer-blind for the liquid formulation versus the lyophilised formulation).

Arms

Are arms mutually exclusive?	Yes
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Arm title	Liq_A Group
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Arm description:

Subjects who received two doses of Porcine circovirus (PCV)-free HRV liquid formulation lot A, at 6 and 12 weeks of age.

Arm type	Experimental
Investigational medicinal product name	HRV PCV-free liquid vaccine formulation lot A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Oral use

Dosage and administration details:

Two oral doses of the HRV vaccines were administered according to a 1-month or 2-months interval according to the immunization schedule for RV vaccine administration in participating countries.

Arm title	Liq_B Group
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Arm description:

Subjects who received two doses of PCV-free HRV liquid formulation lot B, at 6 and 12 weeks of age.

Arm type	Experimental
Investigational medicinal product name	HRV PCV-free liquid vaccine formulation lot B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Oral use

Dosage and administration details:

Two oral doses of the HRV vaccines were administered according to a 1-month or 2-months interval according to the immunization schedule for RV vaccine administration in participating countries.

Arm title	Liq_C Group
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Arm description:

Subjects who received two doses of PCV-free HRV liquid formulation lot C, at 6 and 12 weeks of age.

Arm type	Experimental
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Investigational medicinal product name	HRV PCV-free liquid vaccine formulation lot C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Oral use

Dosage and administration details:

Two oral doses of the HRV vaccines were administered according to a 1-month or 2-months interval according to the immunization schedule for RV vaccine administration in participating countries.

Arm title	Lyo Control Group
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Arm description:

Subjects who received two doses of currently licensed lyophilized HRV vaccine, at 6 and 12 weeks of age.

Arm type	Active comparator
Investigational medicinal product name	HRV vaccine lyophilized formulation
Investigational medicinal product code	BB-IND-16992
Other name	Lyophilised HRV
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Oral use

Dosage and administration details:

Two oral doses of the HRV vaccines were administered according to a 1-month or 2-months interval according to the immunization schedule for RV vaccine administration in participating countries.

Number of subjects in period 1	Liq_A Group	Liq_B Group	Liq_C Group
Started	400	396	402
Completed	386	383	385
Not completed	14	13	17
Migrated/moved from the study area	2	1	2
Consent withdrawn by subject	4	2	7
Not specified	1	-	-
Lost to follow-up	7	10	8

Number of subjects in period 1	Lyo Control Group
Started	402
Completed	391
Not completed	11
Migrated/moved from the study area	1
Consent withdrawn by subject	3
Not specified	-
Lost to follow-up	7

Baseline characteristics

Reporting groups

Reporting group title	Liq_A Group
Reporting group description:	
Subjects who received two doses of Porcine circovirus (PCV)-free HRV liquid formulation lot A, at 6 and 12 weeks of age.	
Reporting group title	Liq_B Group
Reporting group description:	
Subjects who received two doses of PCV-free HRV liquid formulation lot B, at 6 and 12 weeks of age.	
Reporting group title	Liq_C Group
Reporting group description:	
Subjects who received two doses of PCV-free HRV liquid formulation lot C, at 6 and 12 weeks of age.	
Reporting group title	Lyo Control Group
Reporting group description:	
Subjects who received two doses of currently licensed lyophilized HRV vaccine, at 6 and 12 weeks of age.	

Reporting group values	Liq_A Group	Liq_B Group	Liq_C Group
Number of subjects	400	396	402
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	400	396	402
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: weeks			
arithmetic mean	8.5	8.4	8.4
standard deviation	± 1.5	± 1.5	± 1.6
Sex: Female, Male			
Units: Subjects			
Female	208	198	205
Male	192	198	197
Race/Ethnicity, Customized			
Units: Subjects			
American Indian Or Alaska Native	6	2	3
Asian	95	96	98
Black Or African American	6	9	13
Native Hawaiian Or Other Pacific Islander	1	0	0
Other	29	31	26
White	263	258	262

Reporting group values	Lyo Control Group	Total	
Number of subjects	402	1600	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	402	1600	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: weeks			
arithmetic mean	8.5		
standard deviation	± 1.5	-	
Sex: Female, Male Units: Subjects			
Female	203	814	
Male	199	786	
Race/Ethnicity, Customized Units: Subjects			
American Indian Or Alaska Native	5	16	
Asian	95	384	
Black Or African American	13	41	
Native Hawaiian Or Other Pacific Islander	0	1	
Other	27	113	
White	262	1045	

Subject analysis sets

Subject analysis set title	Liq_Pool Group
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects who received two doses of PCV-free HRV liquid formulation of pooled lot A, B and C at 6 and 12 weeks of age.

Reporting group values	Liq_Pool Group		
Number of subjects	984		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	984		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		

Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: weeks			
arithmetic mean	11.65		
standard deviation	± 3.88		
Sex: Female, Male			
Units: Subjects			
Female	500		
Male	484		
Race/Ethnicity, Customized			
Units: Subjects			
American Indian Or Alaska Native	9		
Asian	260		
Black Or African American	16		
Native Hawaiian Or Other Pacific Islander	1		
Other	630		
White	68		

End points

End points reporting groups

Reporting group title	Liq_A Group
Reporting group description: Subjects who received two doses of Porcine circovirus (PCV)-free HRV liquid formulation lot A, at 6 and 12 weeks of age.	
Reporting group title	Liq_B Group
Reporting group description: Subjects who received two doses of PCV-free HRV liquid formulation lot B, at 6 and 12 weeks of age.	
Reporting group title	Liq_C Group
Reporting group description: Subjects who received two doses of PCV-free HRV liquid formulation lot C, at 6 and 12 weeks of age.	
Reporting group title	Lyo Control Group
Reporting group description: Subjects who received two doses of currently licensed lyophilized HRV vaccine, at 6 and 12 weeks of age.	
Subject analysis set title	Liq_Pool Group
Subject analysis set type	Per protocol
Subject analysis set description: Subjects who received two doses of PCV-free HRV liquid formulation of pooled lot A, B and C at 6 and 12 weeks of age.	

Primary: Anti-Rota Virus (Anti-RV) Immunoglobulin A (IgA) antibody concentrations in the Human Rotavirus (HRV) liquid formulation groups (Liq_A, Liq_B and Liq_C)

End point title	Anti-Rota Virus (Anti-RV) Immunoglobulin A (IgA) antibody concentrations in the Human Rotavirus (HRV) liquid formulation groups (Liq_A, Liq_B and Liq_C) ^[1]
End point description: Antibody concentrations against Rota Virus (RV) were determined as Geometric Mean Antibody Concentration (GMC) and expressed as Units per milliliter (U/mL).	
End point type	Primary
End point timeframe: At Month 2-4 (i.e. approximately 1-month or 2-months after the second dose of HRV vaccine according to the immunization schedule for RV vaccine administration in participating countries)	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results for this end point were tabulated to demonstrate the consistency of three lots of PCV-free liquid HRV vaccine in terms of GMC's. This endpoint, therefore, presents the results for groups applicable for this analysis (i.e., Liq_A, Liq_B, and Liq_C Groups).

End point values	Liq_A Group	Liq_B Group	Liq_C Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	332	326	326	
Units: U/mL				
geometric mean (confidence interval 95%)	155.7 (125.6 to 193.1)	147.3 (118.4 to 183.3)	175.9 (142.8 to 216.8)	

Statistical analyses

Statistical analysis title	Lot-to-lot consistency of the HRV vaccine
Statistical analysis description:	
GMC Ratio of Anti-RV IgA antibody for Lot A and Lot B groups was calculated using ANOVA model with vaccine groups and country as fixed effects.	
Comparison groups	Liq_A Group v Liq_B Group
Number of subjects included in analysis	658
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMC Ratio at At Month 2-4
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.44

Statistical analysis title	Lot-to-lot consistency of the HRV vaccine
Statistical analysis description:	
GMC Ratio of Anti-RV IgA antibody for Lot A and Lot C groups was calculated using ANOVA model with vaccine groups and country as fixed effects.	
Comparison groups	Liq_A Group v Liq_C Group
Number of subjects included in analysis	658
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMC Ratio at At Month 2-4
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.19

Statistical analysis title	Lot-to-lot consistency of the HRV vaccine
Statistical analysis description:	
GMC Ratio of Anti-RV IgA antibody for Lot B and Lot C groups was calculated using ANOVA model with vaccine groups and country as fixed effects.	
Comparison groups	Liq_B Group v Liq_C Group
Number of subjects included in analysis	652
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMC Ratio at At Month 2-4
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.11

Primary: Percentage of seroconverted subjects with RV antibody titers above or equal to cut-off value in Porcine Circovirus (PCV) -free liquid HRV vaccine (pooled HRV liquid group) and Control group

End point title	Percentage of seroconverted subjects with RV antibody titers above or equal to cut-off value in Porcine Circovirus (PCV) -free liquid HRV vaccine (pooled HRV liquid group) and Control group ^[2]
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End point description:

Seroconversion rate (SCR) was defined as the percentage of subjects who were initially seronegative (i.e., with anti-RV IgA antibody concentration less than (<) 20 U/mL before the first dose of HRV vaccine) and developed anti-RV IgA antibody concentration greater than or equal to ($\geq$) 20 U/mL at Month 2-4 (1-2 months after dose 2). SCR was analyzed using Enzyme-Linked Immunosorbent Assay (ELISA). The analysis was assessed to demonstrate the immunological non-inferiority of PCV-free liquid HRV vaccine as compared to the currently licensed lyophilized HRV vaccine (pooled HRV liquid groups) in terms of seroconversion rates 1-2 months after Dose 2.

End point type	Primary
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End point timeframe:

At Month 2-4 (i.e. approximately 1-month or 2-months after the second dose of HRV vaccine according to the immunization schedule for RV vaccine administration in participating countries)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results for this end point were tabulated to demonstrate the non-inferiority of Liq_Pool group (for the three pooled lots) compared to Lyo_Control group in terms of seroconversion rates. This endpoint, therefore, presents the results for groups applicable for this analysis (i.e., Liq_Pool and Lyo_Control Groups).

End point values	Lyo Control Group	Liq_Pool Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	329	984		
Units: Percentage of subjects				
number (confidence interval 95%)	81.8 (77.2 to 85.8)	79.3 (76.6 to 81.8)		

Statistical analyses

Statistical analysis title	Non-inferiority of the HRV vaccine
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Statistical analysis description:

Non-inferiority of Pooled HRV liquid group as compared to Control group in terms of the difference in the percentage of subjects with anti-RV IgA titer above or equal to the specified cut off with its

Comparison groups	Lyo Control Group v Liq_Pool Group
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Number of subjects included in analysis	1313
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	SCR difference at Month 2-4
Point estimate	-2.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.15
upper limit	2.63

Primary: Anti-RV IgA antibody concentrations in PCV-free liquid HRV vaccine (pooled HRV liquid group) and Control group

End point title	Anti-RV IgA antibody concentrations in PCV-free liquid HRV vaccine (pooled HRV liquid group) and Control group ^[3]
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End point description:

Antibody concentrations against RV were determined as GMCs and expressed as U/mL. The analysis was assessed to demonstrate the non-inferiority of the PCV-free liquid HRV vaccine (pooled HRV liquid groups) to that of the currently licensed lyophilised HRV vaccine in terms of serum anti-RV IgA antibody concentrations 1-2 months after Dose 2.

End point type	Primary
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End point timeframe:

At Month 2-4 (i.e. approximately 1-month or 2-months after the second dose of HRV vaccine according to the immunization schedule for RV vaccine administration in participating countries)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results for this end point were tabulated to demonstrate the non-inferiority of Liq_Pool group (for the three pooled lots) compared to Lyo_Control group in terms of GMC's. This endpoint, therefore, presents the results for groups applicable for this analysis (i.e., Liq_Pool and Lyo_Control Groups).

End point values	Lyo Control Group	Liq_Pool Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	329	984		
Units: U/mL				
geometric mean (confidence interval 95%)	153.8 (125.1 to 189.0)	159.2 (140.7 to 180.1)		

Statistical analyses

Statistical analysis title	Non-inferiority of the HRV vaccine
Statistical analysis description:	
	Non-inferiority of Pooled HRV liquid group as compared to Control group in terms of the GMC ratio calculated using ANOVA model with vaccine groups and country as fixed effects
Comparison groups	Lyo Control Group v Liq_Pool Group

Number of subjects included in analysis	1313
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMC Ratio at At Month 2-4
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.33

Secondary: Percentage of subjects with Anti-RV IgA concentrations

End point title	Percentage of subjects with Anti-RV IgA concentrations ^[4]
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End point description:

Antibody concentrations ≥ 90 U/mL were determined and expressed as GMCs, assessed for the pooled HRV liquid groups and Control Group. The GMC calculations were performed by taking the anti-log of the mean of the log concentration transformations. The analysis was performed to assess the immunogenicity of the PCV-free liquid HRV vaccine (pooled HRV liquid groups) and the currently licensed lyophilized HRV vaccine, in terms of percentage of subjects with anti-RV IgA antibody concentrations ≥ 90 U/mL 1-2 months after Dose 2.

End point type	Secondary
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End point timeframe:

At Month 2-4 (i.e. approximately 1-month or 2-months after the second dose of HRV vaccine according to the immunization schedule for RV vaccine administration in participating countries)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results for this endpoint were tabulated to assess the immunogenicity of Liq_Pool group (for the three pooled lots) compared to Lyo_Control group. This endpoint, therefore, presents the results for groups applicable for this analysis (i.e., Liq_Pool and Lyo_Control Groups).

End point values	Lyo Control Group	Liq_Pool Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	329	984		
Units: Percentage of subjects				
number (confidence interval 95%)	62.3 (56.8 to 67.6)	63.0 (59.9 to 66.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general Adverse Events (AEs)

End point title	Number of subjects with any solicited general Adverse Events (AEs)
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End point description:

Assessed solicited general AEs were cough/runny nose, diarrhea, fever (defined as temperature $\geq 38.0^{\circ}\text{C}$), irritability/fussiness, loss of appetite and vomiting. Any solicited general AE is defined as any occurrence of the specified symptom, irrespective of intensity grade and relationship to vaccination.

End point type	Secondary
End point timeframe:	
During the 8 days (Day 1 to Day 8) follow-up period after each dose of HRV vaccine	

End point values	Liq_A Group	Liq_B Group	Liq_C Group	Lyo Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	400	396	402	402
Units: Participants				
Any - Cough / Runny Nose - Dose 1	93	91	94	102
Any - Cough / Runny Nose - Dose 2	114	100	94	109
Any - Diarrhea - Dose 1	14	13	8	10
Any - Diarrhea - Dose 2	7	12	8	11
Any - Fever ($\geq 38.0^{\circ}\text{C}$) - Dose 1	24	21	20	23
Any - Fever ($\geq 38.0^{\circ}\text{C}$) - Dose 2	36	36	34	32
Any - Irritability / Fussiness - Dose 1	226	214	209	216
Any - Irritability / Fussiness - Dose 2	191	189	194	194
Any - Loss of appetite - Dose 1	97	93	99	96
Any - Loss of appetite - Dose 2	92	84	78	94
Any - Vomiting - Dose 1	39	51	38	42
Any - Vomiting - Dose 2	25	28	31	34

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited AEs.

End point title	Number of subjects with any unsolicited AEs.
End point description:	
An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any is defined as the occurrence of any unsolicited AE irrespective of its intensity grade and relationship to vaccination.	
End point type	Secondary
End point timeframe:	
During the 31 day (Days 1 to Day 31) follow-up period after HRV vaccination.	

End point values	Liq_A Group	Liq_B Group	Liq_C Group	Lyo Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	400	396	402	402
Units: Participants	183	189	200	184

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any Serious Adverse Events (SAEs)

End point title	Number of subjects with any Serious Adverse Events (SAEs)
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End point description:

SAEs assessed include any untoward medical occurrence that resulted in death, were life-threatening, required hospitalization or prolongation of existing hospitalization or resulted in disability/incapacity.

End point type	Secondary
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End point timeframe:

During the entire study period (Day 1 to Month 7-8)

End point values	Liq_A Group	Liq_B Group	Liq_C Group	Lyo Control Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	400	396	402	402
Units: Participants	21	18	21	18

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: During the 8 days (Day 1 to Day 8) follow-up period after each vaccination. Unsolicited AEs: During the 31 days (Day 1 to Day 31) follow-up period after vaccination. SAEs: Throughout the study period (Day 1 to Month 7-8).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Liq_A Group
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Reporting group description:

Subjects who received two doses of Porcine circovirus (PCV)-free HRV liquid formulation lot A, at 6 and 12 weeks of age.

Reporting group title	Liq_B Group
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Reporting group description:

Subjects who received two doses of PCV-free HRV liquid formulation lot B, at 6 and 12 weeks of age.

Reporting group title	Liq_C Group
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Reporting group description:

Subjects who received two doses of PCV-free HRV liquid formulation lot C, at 6 and 12 weeks of age.

Reporting group title	Lyo Control Group
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Reporting group description:

Subjects who received two doses of currently licensed lyophilised HRV vaccine, at 6 and 12 weeks of age.

Serious adverse events	Liq_A Group	Liq_B Group	Liq_C Group
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 400 (5.25%)	18 / 396 (4.55%)	21 / 402 (5.22%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroblastoma			

subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Infantile spasms			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural hygroma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Milk allergy			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Allergic gastroenteritis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infantile colic			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypoxia			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess jaw			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	4 / 400 (1.00%)	3 / 396 (0.76%)	3 / 402 (0.75%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Conjunctivitis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis enteroviral			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis haemophilus			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			

subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	1 / 400 (0.25%)	3 / 396 (0.76%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 400 (0.25%)	1 / 396 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	6 / 400 (1.50%)	6 / 396 (1.52%)	3 / 402 (0.75%)
occurrences causally related to treatment / all	0 / 6	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 400 (0.25%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	3 / 402 (0.75%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval abscess			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Lyo Control Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 402 (4.48%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to liver			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuroblastoma			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Infantile spasms			

subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural hygroma			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Milk allergy			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Allergic gastroenteritis			

subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infantile colic			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intussusception			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess jaw			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute sinusitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis			
subjects affected / exposed	3 / 402 (0.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Conjunctivitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalitis enteroviral			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			

subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis haemophilus				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metapneumovirus infection				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myelitis				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media acute				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media chronic				

subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumococcal sepsis				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	0 / 402 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 402 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchiolitis				
subjects affected / exposed	2 / 402 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchitis				

subjects affected / exposed	1 / 402 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal abscess			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vulval abscess			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Liq_A Group	Liq_B Group	Liq_C Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	333 / 400 (83.25%)	332 / 396 (83.84%)	338 / 402 (84.08%)
General disorders and administration site conditions			
Crying			
subjects affected / exposed	0 / 400 (0.00%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences (all)	0	2	1
Discomfort			
subjects affected / exposed	0 / 400 (0.00%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences (all)	0	2	1
Fatigue			
subjects affected / exposed	1 / 400 (0.25%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences (all)	1	2	1
Injection site induration			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Injection site mass			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Injection site pain			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	2 / 402 (0.50%)
occurrences (all)	0	0	2
Injection site swelling			
subjects affected / exposed	1 / 400 (0.25%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	1 / 400 (0.25%)	3 / 396 (0.76%)	0 / 402 (0.00%)
occurrences (all)	1	4	0
Pyrexia			
subjects affected / exposed	63 / 400 (15.75%)	61 / 396 (15.40%)	53 / 402 (13.18%)
occurrences (all)	70	66	66
Vaccination site discomfort			

subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Vaccination site pain subjects affected / exposed occurrences (all)	3 / 400 (0.75%) 3	1 / 396 (0.25%) 1	1 / 402 (0.25%) 2
Immune system disorders Anaphylactic reaction subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Hypersensitivity subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Immunisation reaction subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	2 / 402 (0.50%) 2
Milk allergy subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	2 / 402 (0.50%) 2
Reproductive system and breast disorders Balanoposthitis subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Penile adhesion subjects affected / exposed occurrences (all)	2 / 400 (0.50%) 2	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	2 / 400 (0.50%) 2	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Catarrh subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	2 / 396 (0.51%) 2	1 / 402 (0.25%) 1
Cough subjects affected / exposed occurrences (all)	165 / 400 (41.25%) 213	146 / 396 (36.87%) 197	152 / 402 (37.81%) 198
Dysphonia			

subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	2 / 400 (0.50%)	6 / 396 (1.52%)	2 / 402 (0.50%)
occurrences (all)	2	6	2
Nasal obstruction			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Respiratory disorder			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	1 / 400 (0.25%)	1 / 396 (0.25%)	1 / 402 (0.25%)
occurrences (all)	1	1	1
Rhinorrhoea			
subjects affected / exposed	2 / 400 (0.50%)	2 / 396 (0.51%)	6 / 402 (1.49%)
occurrences (all)	2	2	6
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 400 (0.25%)	3 / 396 (0.76%)	1 / 402 (0.25%)
occurrences (all)	2	3	1
Wheezing			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	1	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	2 / 400 (0.50%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	2	0	0

Irritability			
subjects affected / exposed	276 / 400 (69.00%)	265 / 396 (66.92%)	264 / 402 (65.67%)
occurrences (all)	426	408	408
Merycism			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Selective eating disorder			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	2 / 402 (0.50%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Sunburn			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Vaccination complication			
subjects affected / exposed	4 / 400 (1.00%)	3 / 396 (0.76%)	3 / 402 (0.75%)
occurrences (all)	4	3	4
Congenital, familial and genetic disorders			

Ankyloglossia congenital subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Brachycephaly subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Craniosynostosis subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Developmental hip dysplasia subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Gray matter heterotopia subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Hydrocele subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Plagiocephaly subjects affected / exposed occurrences (all)	2 / 400 (0.50%) 2	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Trisomy 21 subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Cardiac disorders Arrhythmia subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Nervous system disorders Depressed level of consciousness subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Drooling subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Febrile convulsion			

subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Seizure subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	2 / 400 (0.50%) 2	0 / 396 (0.00%) 0	2 / 402 (0.50%) 2
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Eye disorders Blepharitis subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Dacryostenosis acquired subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Eye allergy subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Eye discharge subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Ocular hyperaemia			

subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	6 / 400 (1.50%)	3 / 396 (0.76%)	5 / 402 (1.24%)
occurrences (all)	7	3	5
Abdominal pain upper			
subjects affected / exposed	3 / 400 (0.75%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	4	1	0
Abnormal faeces			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Aerophagia			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Anal fissure			
subjects affected / exposed	1 / 400 (0.25%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	6 / 400 (1.50%)	10 / 396 (2.53%)	4 / 402 (1.00%)
occurrences (all)	8	11	5
Diarrhoea			
subjects affected / exposed	38 / 400 (9.50%)	42 / 396 (10.61%)	31 / 402 (7.71%)
occurrences (all)	57	63	45
Enteritis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Epigastric discomfort			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Eructation			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0

Flatulence			
subjects affected / exposed	5 / 400 (1.25%)	3 / 396 (0.76%)	4 / 402 (1.00%)
occurrences (all)	7	4	5
Gastrooesophageal reflux disease			
subjects affected / exposed	9 / 400 (2.25%)	9 / 396 (2.27%)	4 / 402 (1.00%)
occurrences (all)	9	10	4
Haematochezia			
subjects affected / exposed	2 / 400 (0.50%)	0 / 396 (0.00%)	3 / 402 (0.75%)
occurrences (all)	2	0	3
Infantile colic			
subjects affected / exposed	2 / 400 (0.50%)	2 / 396 (0.51%)	2 / 402 (0.50%)
occurrences (all)	2	2	2
Mucous stools			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	2	0
Perianal erythema			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Post-tussive vomiting			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Regurgitation			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	2 / 402 (0.50%)
occurrences (all)	0	1	2
Salivary hypersecretion			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Teething			
subjects affected / exposed	1 / 400 (0.25%)	4 / 396 (1.01%)	3 / 402 (0.75%)
occurrences (all)	1	4	3
Vomiting			
subjects affected / exposed	57 / 400 (14.25%)	68 / 396 (17.17%)	60 / 402 (14.93%)
occurrences (all)	72	85	72
Skin and subcutaneous tissue disorders			
Acne infantile			

subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Asteatosis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	6 / 400 (1.50%)	3 / 396 (0.76%)	3 / 402 (0.75%)
occurrences (all)	6	3	3
Dermatitis atopic			
subjects affected / exposed	2 / 400 (0.50%)	2 / 396 (0.51%)	9 / 402 (2.24%)
occurrences (all)	2	2	9
Dermatitis contact			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	4 / 400 (1.00%)	5 / 396 (1.26%)	8 / 402 (1.99%)
occurrences (all)	4	6	10
Eczema			
subjects affected / exposed	9 / 400 (2.25%)	3 / 396 (0.76%)	8 / 402 (1.99%)
occurrences (all)	10	3	8
Eczema asteatotic			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Eczema infantile			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	1 / 402 (0.25%)
occurrences (all)	0	1	1
Erythema			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Ingrowing nail			

subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Intertrigo			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Mechanical urticaria			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Miliaria			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Perioral dermatitis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	2
Petechiae			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	3 / 400 (0.75%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences (all)	3	2	1
Rash generalised			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Seborrhoea			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	2 / 402 (0.50%)
occurrences (all)	0	1	2
Seborrhoeic dermatitis			
subjects affected / exposed	3 / 400 (0.75%)	3 / 396 (0.76%)	1 / 402 (0.25%)
occurrences (all)	3	3	1
Skin lesion			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Urticaria			

subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Renal and urinary disorders Crystalluria subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Musculoskeletal and connective tissue disorders Acquired plagiocephaly subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Head deformity subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Torticollis subjects affected / exposed occurrences (all)	2 / 400 (0.50%) 2	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Infections and infestations Acarodermatitis subjects affected / exposed occurrences (all)	1 / 400 (0.25%) 1	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Acute sinusitis subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	0 / 402 (0.00%) 0
Anal abscess subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	1 / 396 (0.25%) 1	0 / 402 (0.00%) 0
Anal candidiasis subjects affected / exposed occurrences (all)	0 / 400 (0.00%) 0	0 / 396 (0.00%) 0	1 / 402 (0.25%) 1
Bronchiolitis			

subjects affected / exposed	10 / 400 (2.50%)	10 / 396 (2.53%)	7 / 402 (1.74%)
occurrences (all)	10	11	7
Bronchitis			
subjects affected / exposed	5 / 400 (1.25%)	4 / 396 (1.01%)	6 / 402 (1.49%)
occurrences (all)	5	4	6
Bronchitis bacterial			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	1 / 400 (0.25%)	3 / 396 (0.76%)	1 / 402 (0.25%)
occurrences (all)	1	3	1
Conjunctivitis			
subjects affected / exposed	7 / 400 (1.75%)	5 / 396 (1.26%)	11 / 402 (2.74%)
occurrences (all)	7	5	11
Conjunctivitis bacterial			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	1	0	1
Conjunctivitis viral			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	1	0	1
Croup infectious			
subjects affected / exposed	2 / 400 (0.50%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences (all)	2	2	1
Ear infection			
subjects affected / exposed	1 / 400 (0.25%)	3 / 396 (0.76%)	3 / 402 (0.75%)
occurrences (all)	1	3	3
Fungal infection			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 400 (0.00%)	2 / 396 (0.51%)	0 / 402 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	9 / 400 (2.25%)	6 / 396 (1.52%)	3 / 402 (0.75%)
occurrences (all)	9	6	5
Hand-foot-and-mouth disease			

subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Herpangina			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	2 / 400 (0.50%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	4 / 400 (1.00%)	4 / 396 (1.01%)	2 / 402 (0.50%)
occurrences (all)	4	5	2
Laryngitis			
subjects affected / exposed	2 / 400 (0.50%)	1 / 396 (0.25%)	2 / 402 (0.50%)
occurrences (all)	2	1	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	24 / 400 (6.00%)	25 / 396 (6.31%)	36 / 402 (8.96%)
occurrences (all)	25	26	40
Oral candidiasis			
subjects affected / exposed	3 / 400 (0.75%)	2 / 396 (0.51%)	3 / 402 (0.75%)
occurrences (all)	3	2	3
Oral fungal infection			
subjects affected / exposed	3 / 400 (0.75%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	3	0	1
Oral herpes			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	2 / 400 (0.50%)	5 / 396 (1.26%)	4 / 402 (1.00%)
occurrences (all)	2	6	4
Otitis media acute			
subjects affected / exposed	2 / 400 (0.50%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences (all)	2	2	1
Paronychia			

subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 400 (0.25%)	1 / 396 (0.25%)	3 / 402 (0.75%)
occurrences (all)	1	1	3
Pneumonia			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 400 (0.00%)	3 / 396 (0.76%)	0 / 402 (0.00%)
occurrences (all)	0	3	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	1 / 402 (0.25%)
occurrences (all)	0	1	1
Respiratory tract infection			
subjects affected / exposed	2 / 400 (0.50%)	8 / 396 (2.02%)	4 / 402 (1.00%)
occurrences (all)	3	13	4
Respiratory tract infection viral			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	3 / 400 (0.75%)	7 / 396 (1.77%)	6 / 402 (1.49%)
occurrences (all)	5	7	6
Skin bacterial infection			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Streptococcal infection			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Subglottic laryngitis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	2 / 402 (0.50%)
occurrences (all)	0	0	2

Tracheobronchitis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	31 / 400 (7.75%)	34 / 396 (8.59%)	31 / 402 (7.71%)
occurrences (all)	33	38	36
Urinary tract infection			
subjects affected / exposed	0 / 400 (0.00%)	2 / 396 (0.51%)	2 / 402 (0.50%)
occurrences (all)	0	2	2
Viral infection			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	1 / 402 (0.25%)
occurrences (all)	0	1	1
Viral rash			
subjects affected / exposed	2 / 400 (0.50%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 400 (0.75%)	3 / 396 (0.76%)	2 / 402 (0.50%)
occurrences (all)	3	3	2
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Abnormal weight gain			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Appetite disorder			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	145 / 400 (36.25%)	133 / 396 (33.59%)	139 / 402 (34.58%)
occurrences (all)	192	177	177
Feeding disorder			
subjects affected / exposed	2 / 400 (0.50%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	2	0	0
Lactose intolerance			

subjects affected / exposed	0 / 400 (0.00%)	2 / 396 (0.51%)	1 / 402 (0.25%)
occurrences (all)	0	2	1
Malnutrition			
subjects affected / exposed	1 / 400 (0.25%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	1	0	0
Poor feeding infant			
subjects affected / exposed	0 / 400 (0.00%)	0 / 396 (0.00%)	1 / 402 (0.25%)
occurrences (all)	0	0	1
Underweight			
subjects affected / exposed	0 / 400 (0.00%)	1 / 396 (0.25%)	0 / 402 (0.00%)
occurrences (all)	0	1	0
Weight gain poor			
subjects affected / exposed	2 / 400 (0.50%)	0 / 396 (0.00%)	0 / 402 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Lyo Control Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	338 / 402 (84.08%)		
General disorders and administration site conditions			
Crying			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Discomfort			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Injection site induration			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Injection site mass			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Injection site pain			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Injection site swelling			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	55 / 402 (13.68%)		
occurrences (all)	62		
Vaccination site discomfort			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Vaccination site pain			
subjects affected / exposed	4 / 402 (1.00%)		
occurrences (all)	4		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Hypersensitivity			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Immunisation reaction			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Milk allergy			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Penile adhesion			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Catarrh			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	3		
Cough			
subjects affected / exposed	163 / 402 (40.55%)		
occurrences (all)	214		
Dysphonia			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	5 / 402 (1.24%)		
occurrences (all)	5		
Nasal obstruction			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Respiratory disorder			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			

subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	3		
Upper respiratory tract inflammation			
subjects affected / exposed	3 / 402 (0.75%)		
occurrences (all)	3		
Wheezing			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	261 / 402 (64.93%)		
occurrences (all)	419		
Mercism			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Selective eating disorder			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Arthropod sting			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Contusion			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Sunburn			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Vaccination complication			
subjects affected / exposed	6 / 402 (1.49%)		
occurrences (all)	6		
Congenital, familial and genetic disorders			
Ankyloglossia congenital			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Brachycephaly			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Craniosynostosis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Developmental hip dysplasia			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Gray matter heterotopia			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Hydrocele			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Plagiocephaly			

subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Trisomy 21 subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Cardiac disorders Arrhythmia subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Nervous system disorders Depressed level of consciousness subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Droling subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Febrile convulsion subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Seizure subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Somnolence subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Eye disorders Blepharitis subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		

Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Dacryostenosis acquired subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Eye allergy subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Eye discharge subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	7 / 402 (1.74%) 7		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Abnormal faeces subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Aerophagia subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Anal fissure			

subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	8 / 402 (1.99%)		
occurrences (all)	9		
Diarrhoea			
subjects affected / exposed	44 / 402 (10.95%)		
occurrences (all)	59		
Enteritis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Epigastric discomfort			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Eructation			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	8 / 402 (1.99%)		
occurrences (all)	9		
Gastrooesophageal reflux disease			
subjects affected / exposed	11 / 402 (2.74%)		
occurrences (all)	11		
Haematochezia			
subjects affected / exposed	3 / 402 (0.75%)		
occurrences (all)	3		
Infantile colic			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Mucous stools			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Perianal erythema			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Post-tussive vomiting			

subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Regurgitation			
subjects affected / exposed	3 / 402 (0.75%)		
occurrences (all)	3		
Salivary hypersecretion			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Teething			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	65 / 402 (16.17%)		
occurrences (all)	81		
Skin and subcutaneous tissue disorders			
Acne infantile			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Asteatosis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Blister			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	4 / 402 (1.00%)		
occurrences (all)	4		
Dermatitis atopic			
subjects affected / exposed	4 / 402 (1.00%)		
occurrences (all)	4		
Dermatitis contact			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Dermatitis diaper			
subjects affected / exposed	6 / 402 (1.49%)		
occurrences (all)	6		

Eczema			
subjects affected / exposed	7 / 402 (1.74%)		
occurrences (all)	8		
Eczema asteatotic			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Eczema infantile			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Ingrowing nail			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Intertrigo			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Mechanical urticaria			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Miliaria			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Perioral dermatitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Petechiae			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	4 / 402 (1.00%)		
occurrences (all)	4		

Rash generalised subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Seborrhoea subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Skin lesion subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Renal and urinary disorders Crystalluria subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Musculoskeletal and connective tissue disorders Acquired plagiocephaly subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Head deformity subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	0 / 402 (0.00%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	1 / 402 (0.25%) 1		
Torticollis			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Acute sinusitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Anal abscess			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Anal candidiasis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Bronchiolitis			
subjects affected / exposed	9 / 402 (2.24%)		
occurrences (all)	9		
Bronchitis			
subjects affected / exposed	4 / 402 (1.00%)		
occurrences (all)	4		
Bronchitis bacterial			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Candida infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	11 / 402 (2.74%)		
occurrences (all)	12		
Conjunctivitis bacterial			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Conjunctivitis viral			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		

Croup infectious			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Fungal infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Fungal skin infection			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	3 / 402 (0.75%)		
occurrences (all)	5		
Hand-foot-and-mouth disease			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Herpangina			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Impetigo			
subjects affected / exposed	3 / 402 (0.75%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	6 / 402 (1.49%)		
occurrences (all)	6		
Laryngitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	29 / 402 (7.21%)		
occurrences (all)	37		

Oral candidiasis			
subjects affected / exposed	8 / 402 (1.99%)		
occurrences (all)	8		
Oral fungal infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Otitis media acute			
subjects affected / exposed	5 / 402 (1.24%)		
occurrences (all)	5		
Paronychia			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	8 / 402 (1.99%)		
occurrences (all)	9		
Respiratory tract infection viral			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	6 / 402 (1.49%)		
occurrences (all)	6		
Skin bacterial infection			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Streptococcal infection			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Subglottic laryngitis			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Tracheobronchitis			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	30 / 402 (7.46%)		
occurrences (all)	32		
Urinary tract infection			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Viral infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Viral rash			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Vulvovaginal candidiasis			

subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Abnormal weight gain			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Appetite disorder			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	141 / 402 (35.07%)		
occurrences (all)	191		
Feeding disorder			
subjects affected / exposed	2 / 402 (0.50%)		
occurrences (all)	2		
Lactose intolerance			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Malnutrition			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Poor feeding infant			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Underweight			
subjects affected / exposed	0 / 402 (0.00%)		
occurrences (all)	0		
Weight gain poor			
subjects affected / exposed	1 / 402 (0.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2017	The protocol was amended to include the text related to the unapproved medical devices and incidents associated with it as per Japan-specific requirements.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported