



Clinical trial results:

A phase III, double-blind, randomized, placebo-controlled, multi-country and multi-center study to assess the efficacy and safety of two doses of GSK Biologicals' oral live attenuated human rotavirus (HRV) vaccine in healthy infants.

Summary

EudraCT number	2015-001541-92
Trial protocol	Outside EU/EEA
Global end of trial date	07 July 2008

Results information

Result version number	v2 (current)
This version publication date	10 August 2016
First version publication date	02 August 2015
Version creation reason	<ul style="list-style-type: none">• New data added to full data set Full disclosure of data set

Trial information

Trial identification

Sponsor protocol code	444563/028/029/030,107070,72,76
-----------------------	---------------------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00329745
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trails Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trails Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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	19 January 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2008
Global end of trial reached?	Yes
Global end of trial date	07 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- In all subjects, to determine if two doses of GSK Biologicals' HRV vaccine given concomitantly with routine vaccinations* can prevent severe rotavirus gastroenteritis (RV GE) caused by the circulating wild-type RV strains during the period starting from 2 weeks after Dose 2 until 2 years of age. (*Whenever Oral Polio Vaccination (OPV) is used a minimum 2-week interval should be observed between HRV vaccine and OPV doses.)
- In all subjects, to assess the safety of HRV vaccine with respect to definite intussusception (IS) within 31 days (Day 0-Day 30) after each HRV vaccine dose.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2003
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hong Kong: 3025
Country: Number of subjects enrolled	Taiwan: 1141
Country: Number of subjects enrolled	Singapore: 6542
Worldwide total number of subjects	10708
EEA total number of subjects	0

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	10708

months)	
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: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	Primary study (up to Visit 5)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotarix Group

Arm description:

During the primary study (NCT00197210) subjects received two oral doses of Rotarix™ vaccine.

Arm type	Experimental
Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Oral use

Dosage and administration details:

Oral administration, 2 doses

Arm title	Placebo Group
------------------	---------------

Arm description:

During the primary study (NCT00197210) subjects received two oral doses of placebo.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Oral use

Dosage and administration details:

Oral administration, 2 doses

Number of subjects in period 1	Rotarix Group	Placebo Group
Started	5359	5349
Completed	5215	5170
Not completed	144	179
Adverse event, serious fatal	3	8
Consent withdrawn by subject	40	53
Adverse event, non-fatal	4	2
Conflict of interest	1	-
Lost to follow-up	93	111
Due to undescended testis	1	-
Protocol deviation	2	5

Period 2

Period 2 title	Follow-up (up to Visit 6)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotarix Group

Arm description:

During the primary study (NCT00197210) subjects received two oral doses of Rotarix™ vaccine.

Arm type	Experimental
Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Oral use

Dosage and administration details:

Oral administration, 2 doses

Arm title	Placebo Group
------------------	---------------

Arm description:

During the primary study (NCT00197210) subjects received two oral doses of placebo.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Oral use

Dosage and administration details:

Oral administration, 2 doses

Number of subjects in period 2^[1]	Rotarix Group	Placebo Group
Started	4359	4328
Completed	4272	4226
Not completed	87	102
Consent withdrawn by subject	-	1
Lost to follow-up	86	101
Protocol deviation	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Some subjects who completed the study up to Visit 5, did not come back for the Visit 6 of the study.

Baseline characteristics

Reporting groups

Reporting group title	Rotarix Group
Reporting group description:	
During the primary study (NCT00197210) subjects received two oral doses of Rotarix™ vaccine.	
Reporting group title	Placebo Group
Reporting group description:	
During the primary study (NCT00197210) subjects received two oral doses of placebo.	

Reporting group values	Rotarix Group	Placebo Group	Total
Number of subjects	5359	5349	10708
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)			0
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: months			
arithmetic mean	23.2	23.2	
standard deviation	± 2.31	± 2.51	-
Gender categorical Units: Subjects			
Female	2631	2625	5256
Male	2728	2724	5452

End points

End points reporting groups

Reporting group title	Rotarix Group
Reporting group description: During the primary study (NCT00197210) subjects received two oral doses of Rotarix™ vaccine.	
Reporting group title	Placebo Group
Reporting group description: During the primary study (NCT00197210) subjects received two oral doses of placebo.	
Reporting group title	Rotarix Group
Reporting group description: During the primary study (NCT00197210) subjects received two oral doses of Rotarix™ vaccine.	
Reporting group title	Placebo Group
Reporting group description: During the primary study (NCT00197210) subjects received two oral doses of placebo.	

Primary: Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the wild RV strains.

End point title	Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the wild RV strains.
End point description: Severe GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Primary
End point timeframe: From 2 weeks after Dose 2 up to Visit 5 (two years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	2	51		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description: Vaccine efficacy with respect to severe RV GE caused by the wild RV strains. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group

Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	96.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	85.1
upper limit	99.5

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)
End point description:	
An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.	
End point type	Secondary
End point timeframe:	
From Visit 5 (Month 21-22) until study end (Month 33-34)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4359	4328		
Units: Subjects				
Any SAE(s)	10	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe RV GE caused by the wild RV strain of type G1

End point title	Number of subjects with severe RV GE caused by the wild RV strain of type G1
End point description:	
Severe GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe:	
From 2 weeks after Dose 2 up to Visit 5 (two years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	0	21		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE caused by the wild RV strain of type G1. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo	
Comparison groups	Placebo Group v Rotarix Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	80.8
upper limit	100

Secondary: Number of subjects with severe RV GE due to non-G1 types

End point title	Number of subjects with severe RV GE due to non-G1 types
End point description:	
Severe GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe:	
From 2 weeks after Dose 2 up to Visit 5 (two years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects				
Pooled non-G1 type	2	31		
G2+P4 wild-type	0	2		
G3+P8 wild-type	1	18		
G9+P8 wild-type	1	12		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE due to pooled non-G1 type. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	93.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	74.7
upper limit	99.3

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE due to G2+P4 wild-type. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.25
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-431.7
upper limit	100

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE due to G3+P8 wild-type. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	94.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	64.9
upper limit	99.9

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE due to G9+P8 wild-type. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	91.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	43.8
upper limit	99.8

Secondary: Number of subjects with severe RV GE by the circulating wild-type RV strains

End point title	Number of subjects with severe RV GE by the circulating wild-type RV strains
-----------------	--

End point description:

Subjects with severe RV GE caused by the wild RV strain of G1 type, due to non-G1 types and due to each non-G1 type. Severe GE was defined as a gastroenteritis episode requiring hospitalization and/or

re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.

End point type	Secondary
End point timeframe:	
From Dose 1 up to Visit 5 (two years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5359	5349		
Units: Subjects				
G1 wild-type + P8 wild-type	0	22		
G2 + P4 wild-type	0	2		
G3 + P8 wild-type	1	18		
G9 + P8 wild-type	1	14		
Pooled non-G1	2	33		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE caused by wild RV strain of G1 type. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10708
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	81.8
upper limit	100

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE caused by non-G1 types (pooled non-G1). Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group

Number of subjects included in analysis	10708
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	94
Confidence interval	
level	95 %
sides	2-sided
lower limit	76.3
upper limit	99.3

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
-----------------------------------	---

Statistical analysis description:

Vaccine efficacy with respect to severe RV GE caused by each non-G1 type (G2 + P4 wild-type). Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10708
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.25
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-431.5
upper limit	100

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
-----------------------------------	---

Statistical analysis description:

Vaccine efficacy with respect to severe RV GE caused by non-G1 type (G3 + P8 wild-type). Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10708
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	94.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	64.9
upper limit	99.9

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
-----------------------------------	---

Statistical analysis description:

Vaccine efficacy with respect to severe RV GE caused by non-G1 type (G9 + P8 wild-type). Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10708
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	92.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.1
upper limit	99.8

Secondary: Number of subjects with RV GE episodes caused by the circulating wild-type RV strains and requiring hospitalization and/or re-hydration therapy

End point title	Number of subjects with RV GE episodes caused by the circulating wild-type RV strains and requiring hospitalization and/or re-hydration therapy
-----------------	---

End point description:

Gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.

End point type	Secondary
----------------	-----------

End point timeframe:

From 2 weeks after Dose 2 up to Visit 5 (two years of age)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	3	52		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to RV GE
Statistical analysis description: Vaccine efficacy with respect to RV GE caused by circulating wild-type RV strains. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	94.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	82.2
upper limit	98.8

Secondary: Number of subjects with severe RV GE caused by the circulating wild-type RV strains

End point title	Number of subjects with severe RV GE caused by the circulating wild-type RV strains
End point description: Severe RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe: After Visit 4 (one year of age) up to Visit 5 (two years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5221	5194		
Units: Subjects	2	36		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description: Vaccine efficacy with respect to severe RV GE caused by circulating wild-type RV strains. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group

Number of subjects included in analysis	10415
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	94.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	78.5
upper limit	99.4

Secondary: Number of subjects with severe RV GE caused by the circulating wild-type RV strains

End point title	Number of subjects with severe RV GE caused by the circulating wild-type RV strains
End point description: Severe RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale	
End point type	Secondary
End point timeframe: From 2 weeks after Dose 2 up to Visit 4 (one year of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	0	15		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description: Vaccine efficacy with respect to severe RV GE caused by the circulating wild-type RV strains. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100

Confidence interval	
level	95 %
sides	2-sided
lower limit	72.2
upper limit	100

Secondary: Number of subjects with severe GE of any etiology

End point title	Number of subjects with severe GE of any etiology
End point description:	
Severe GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe:	
From 2 weeks after Dose 2 up to Visit 5 (two years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	141	202		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe GE
Statistical analysis description:	
Vaccine efficacy with respect to severe GE of any etiology. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	30.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.1
upper limit	44.2

Secondary: Number of subjects with severe RV GE caused by the wild RV strains

End point title	Number of subjects with severe RV GE caused by the wild RV strains
End point description: Severe RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe: From 2 weeks after Dose 2 up to Visit 6 (three years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	2	64		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description: Vaccine efficacy with respect to severe RV GE caused by wild RV strains. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	96.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	88.3
upper limit	99.6

Secondary: Number of subjects with severe RV GE caused by the wild RV strain of G1 type

End point title	Number of subjects with severe RV GE caused by the wild RV strain of G1 type
End point description: Severe RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary

End point timeframe:

From 2 weeks after Dose 2 up to Visit 6 (three years of age)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	0	26		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
----------------------------	---

Statistical analysis description:

Vaccine efficacy with respect to severe RV GE caused by the wild RV strain of G1 type. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	84.8
upper limit	100

Secondary: Number of subjects with severe RV GE due to non-G1 types

End point title	Number of subjects with severe RV GE due to non-G1 types
-----------------	--

End point description:

Severe RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.

End point type	Secondary
----------------	-----------

End point timeframe:

From 2 weeks after Dose 2 up to Visit 6 (three years of age)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	2	39		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE due to non-G1 types. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	94.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	80.2
upper limit	99.4

Secondary: Number of subjects with severe RV GE due to each non-G1 type

End point title	Number of subjects with severe RV GE due to each non-G1 type
End point description:	
Severe RV GE caused by each non-G1 type such as G2, G3 and G9. Severe RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe:	
From 2 weeks after Dose 2 up to Visit 6 (three years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects				
G2 type	0	4		
G3 type	1	22		
G9 type	1	14		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE caused by non-G1 type (G2 type). Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.062
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.3
upper limit	100

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE due to non-G1 type (G3 type). Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	95.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	71.9
upper limit	99.9

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
-----------------------------------	---

Statistical analysis description:

Vaccine efficacy with respect to severe RV GE due to non-G1 type (G9 type). Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	92.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.1
upper limit	99.8

Secondary: Number of subjects with RV GE caused by the circulating wild-type RV strains and requiring hospitalization and/or re-hydration therapy

End point title	Number of subjects with RV GE caused by the circulating wild-type RV strains and requiring hospitalization and/or re-hydration therapy
-----------------	--

End point description:

RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.

End point type	Secondary
----------------	-----------

End point timeframe:

From 2 weeks after Dose 2 up to Visit 6 (three years of age)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	3	67		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to RV GE
-----------------------------------	--

Statistical analysis description:

Vaccine efficacy with respect to RV GE caused by circulating wild-type RV strains and requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
-------------------	-------------------------------

Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	95.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	86.4
upper limit	99.1

Secondary: Number of subjects with severe RV GE caused by the circulating wild-type RV strains

End point title	Number of subjects with severe RV GE caused by the circulating wild-type RV strains
End point description:	Severe RV GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.
End point type	Secondary
End point timeframe:	From Visit 5 (two years of age) to Visit 6 (three years of age)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4222	4185		
Units: Subjects	0	13		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	Vaccine efficacy with respect to severe RV GE caused by the circulating wild-type RV strains. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	8407
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	100

Confidence interval	
level	95 %
sides	2-sided
lower limit	67.5
upper limit	100

Secondary: Number of subjects with severe GE of any etiology

End point title	Number of subjects with severe GE of any etiology
End point description:	
Severe GE was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe:	
From 2 weeks after Dose 2 up to Visit 6 (three years of age)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5263	5256		
Units: Subjects	192	262		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe GE
Statistical analysis description:	
Vaccine efficacy with respect to severe GE of any etiology. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.	
Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	10519
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	26.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.5
upper limit	39.6

Secondary: Number of subjects with Anti-rotavirus IgA seroconversion rates above

the cut-off value

End point title	Number of subjects with Anti-rotavirus IgA seroconversion rates above the cut-off value
-----------------	---

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titre \geq cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject was defined as a subject whose titer was below the cut-off value (20 U/mL)

End point type	Secondary
----------------	-----------

End point timeframe:

At Visit 1 (Day 0, pre-vaccination [Pre]) and Visit 3 (Month 2-4 [M2-4])

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	124		
Units: Subjects				
Pre	0	0		
PII(M2-4)	108	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rotavirus IgA antibody Geometric Mean Concentrations (GMCs)

End point title	Anti-rotavirus IgA antibody Geometric Mean Concentrations (GMCs)
-----------------	--

End point description:

Antibody concentrations below the cut-off (20 U/mL) of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
----------------	-----------

End point timeframe:

At Visit 1 (Day 0, pre-vaccination [Pre]) and Visit 3 (Month 2-4 [M2-4])

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	124		
Units: U/mL				
geometric mean (confidence interval 95%)				
Pre	0 (0 to 0)	0 (0 to 0)		
PII(M2-4)	238.6 (183.4 to 310.3)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-rotavirus IgA seroconversion rates above the cut-off value by country

End point title	Number of subjects with Anti-rotavirus IgA seroconversion rates above the cut-off value by country
-----------------	--

End point description:

Seroconversion is defined as the appearance of antibodies (i.e. titre \geq cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject was defined as a subject whose titer was below the cut-off value (20 U/mL). The results are listed for a subset of 100 subjects per country- Singapore, Hong Kong and Taiwan.

End point type	Secondary
----------------	-----------

End point timeframe:

At Visit 1 (Day 0, pre-vaccination [Pre]) and Visit 3 (Month 2-4 [M2-4])

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	46		
Units: Subjects				
Singapore; Pre [N= 40, 46]	0	0		
Singapore; PII(M2-4) [N= 40, 46]	39	1		
Hong Kong; Pre [N= 40, 43]	0	0		
Hong Kong; PII(M2-4) [N= 40, 43]	39	0		
Taiwan; Pre [N= 35, 35]	0	0		
Taiwan; PII(M2-4) [N= 35, 35]	30	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rotavirus IgA antibody Geometric Mean Concentrations (GMCs)

End point title	Anti-rotavirus IgA antibody Geometric Mean Concentrations (GMCs)
-----------------	--

End point description:

Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. The

End point type	Secondary
----------------	-----------

End point timeframe:

At Visit 1 (Day 0, pre-vaccination [Pre]) and Visit 3 (Month 2-4 [M2-4])

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	46		
Units: U/mL				
geometric mean (confidence interval 95%)				
Singapore; Pre [N= 40, 46]	0 (0 to 0)	0 (0 to 0)		
Singapore; PII(M2-4) [N= 40, 46]	368.5 (231 to 588)	0 (0 to 0)		
Hong Kong; Pre [N= 40, 43]	0 (0 to 0)	0 (0 to 0)		
Hong Kong; PII(M2-4) [N= 40, 43]	314.6 (215.1 to 460.1)	0 (0 to 0)		
Taiwan; Pre [N= 35, 35]	0 (0 to 0)	0 (0 to 0)		
Taiwan; PII(M2-4) [N= 35, 35]	105.8 (67.4 to 166.2)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with definite Intussusception (IS)

End point title	Number of subjects with definite Intussusception (IS)
End point description:	
The diagnosis of IS was confirmed on the demonstration of invagination of the intestine at surgery or autopsy, or by using radiologic techniques: gas/liquid contrast enema or abdominal ultrasound.	
End point type	Secondary
End point timeframe:	
From Dose 1 (Day 0) up to Visit 3 (Month 2-4), Visit 4 (Month 9-10) and Visit 5 (Month 21-22).	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5359	5349		
Units: Subjects				
Dose 1 to Visit 3	0	0		
Dose 1 to Visit 4	3	2		
Dose 1 to Visit 5	8	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)
End point description:	
An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires	

hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary
End point timeframe:	
From Dose 1 (Day 0) until Visit 5 (Month 21-22)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5359	5349		
Units: Subjects				
Any SAE(s)	1001	1098		
Fatal SAE(s)	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe RV GE caused by the circulating wild-type RV strain

End point title	Number of subjects with severe RV GE caused by the circulating wild-type RV strain
End point description:	
Severe GE is defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility with a score of 11 or greater on the Vesikari scale.	
End point type	Secondary
End point timeframe:	
From Dose 1 (Day 0) up to Visit 5 (Month 21-22)	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5359	5349		
Units: Subjects	2	54		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RV GE
Statistical analysis description:	
Vaccine efficacy with respect to severe RV GE caused by the circulating wild-type RV strains. Vaccine efficacy was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo	
Comparison groups	Rotarix Group v Placebo Group

Number of subjects included in analysis	10708
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	percent reduction
Point estimate	96.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	86
upper limit	99.6

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Serious adverse events (SAEs): from Dose 1 until Visit 5 and from Visit 5 until study end.

Adverse event reporting additional description:

Adverse events were not systematically followed up in this study. Only the adverse events (and serious adverse events) leading to subject withdrawal or drop-out were collected. The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	11.1
--------------------	------

Reporting groups

Reporting group title	Rotarix Group
-----------------------	---------------

Reporting group description:

During the primary study (NCT00197210) subjects received two oral doses of Rotarix™ vaccine.

Reporting group title	Placebo Group
-----------------------	---------------

Reporting group description:

During the primary study (NCT00197210) subjects received two oral doses of placebo.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events were planned to be assessed in this study as per the protocol.

Serious adverse events	Rotarix Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	171 / 5359 (3.19%)	186 / 5349 (3.48%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukemia			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephroblastoma			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Circumcision			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	9 / 5359 (0.17%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia repair			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Developmental delay			
subjects affected / exposed	1 / 5359 (0.02%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hyperpyrexia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritability			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ disorder			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	11 / 5359 (0.21%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 11	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden infant death syndrome (non-fatal SAE)			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden infant death syndrome (fatal SAE)	Additional description: This reported SAE is a fatal SAE.		
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Milk allergy			
subjects affected / exposed	3 / 5359 (0.06%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Child abuse			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Physical abuse			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Balanitis			
subjects affected / exposed	1 / 5359 (0.02%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balanoposthitis			
subjects affected / exposed	2 / 5359 (0.04%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal swelling			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration (non-fatal SAE)			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			

subjects affected / exposed	23 / 5359 (0.43%)	27 / 5349 (0.50%)	
occurrences causally related to treatment / all	0 / 23	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnea			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemoptysis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile asthma			

subjects affected / exposed	0 / 5359 (0.00%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease (non-fatal SAE)			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis allergic			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration (fatal SAE)	Additional description: This reported SAE is a fatal SAE.		
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease (fatal SAE)	Additional description: This reported SAE is a fatal SAE.		

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Breath holding			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crying			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased activity			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Body height abnormal			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac murmur functional			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical observation			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Burns third degree			
subjects affected / exposed ^[2]	1 / 4359 (0.02%)	0 / 4328 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious (Visit 5 to Visit 6)			
subjects affected / exposed ^[3]	0 / 4359 (0.00%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose (Visit 5 to Visit 6)			
subjects affected / exposed ^[4]	0 / 4359 (0.00%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental drug intake by child			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental exposure			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental poisoning			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropod bite			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns first degree			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Caustic injury			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug toxicity			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body trauma			
subjects affected / exposed	3 / 5359 (0.06%)	8 / 5349 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			

subjects affected / exposed	0 / 5359 (0.00%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	36 / 5359 (0.67%)	32 / 5349 (0.60%)	
occurrences causally related to treatment / all	0 / 36	0 / 32	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	3 / 5359 (0.06%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb crushing injury			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth injury			

subjects affected / exposed	3 / 5359 (0.06%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open wound			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose (Visit 1 to Visit 5)			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	4 / 5359 (0.07%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	6 / 5359 (0.11%)	6 / 5349 (0.11%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth fracture			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaccination complication			
subjects affected / exposed	0 / 5359 (0.00%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Ankyloglossia congenital			
subjects affected / exposed	2 / 5359 (0.04%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial septal defect			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cleft palate			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital epiblepharon			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cryptorchism			
subjects affected / exposed	2 / 5359 (0.04%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal atresia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysmorphism			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngomalacia			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangioma			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcephaly			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patent ductus arteriosus			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Preauricular cyst			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyloric stenosis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinoblastoma			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalassaemia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial tachycardia			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac aneurysm			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomegaly			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wolff-Parkinson-white syndrome			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion (Visit 5 to Visit 6)			
subjects affected / exposed ^[5]	1 / 4359 (0.02%)	0 / 4328 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arachnoid cyst			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign intracranial hypertension			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain damage			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain edema			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral hemorrhage			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	17 / 5359 (0.32%)	10 / 5349 (0.19%)	
occurrences causally related to treatment / all	0 / 17	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyskinesia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 5359 (0.02%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial palsy			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion (Visit 1 to Visit 5)			

subjects affected / exposed	73 / 5359 (1.36%)	66 / 5349 (1.23%)
occurrences causally related to treatment / all	0 / 73	0 / 66
deaths causally related to treatment / all	0 / 0	0 / 0
Guillain-barre syndrome		
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Head titubation		
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intraventricular hemorrhage		
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ischaemic stroke		
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Muscle spasticity		
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Myoclonus		
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Partial seizures		
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Somnolence		

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Idiopathic thrombocytopenic purpura (Visit 5 to Visit 6)			
subjects affected / exposed ^[6]	0 / 4359 (0.00%)	2 / 4328 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis (Visit 5 to Visit 6)			
subjects affected / exposed ^[7]	1 / 4359 (0.02%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anemia			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anemia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic thrombocytopenic purpura (Visit 1 to Visit 5)			
subjects affected / exposed	2 / 5359 (0.04%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anemia			

subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anemia			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 5359 (0.00%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	1 / 5359 (0.02%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye discharge			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye swelling			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strabismus			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception (Visit 5 to Visit 6)			
subjects affected / exposed ^[8]	2 / 4359 (0.05%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis (Visit 5 to Visit 6)			
subjects affected / exposed ^[9]	1 / 4359 (0.02%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal discomfort			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	3 / 5359 (0.06%)	6 / 5349 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	6 / 5359 (0.11%)	8 / 5349 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	3 / 5359 (0.06%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea hemorrhagic			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	6 / 5359 (0.11%)	6 / 5349 (0.11%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Frequent bowel movements			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis (Visit 1 to Visit 5)			
subjects affected / exposed	12 / 5359 (0.22%)	15 / 5349 (0.28%)	
occurrences causally related to treatment / all	0 / 12	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastro esophageal reflux disease			

subjects affected / exposed	0 / 5359 (0.00%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingivitis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematemesis			
subjects affected / exposed	2 / 5359 (0.04%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematochezia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception (Visit 1 to Visit 5)			

subjects affected / exposed	8 / 5359 (0.15%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Megacolon			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth ulceration			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 5359 (0.06%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatomegaly			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatosplenomegaly			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinemia			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic (Visit 5 to Visit 6)			
subjects affected / exposed ^[10]	1 / 4359 (0.02%)	0 / 4328 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	0 / 5359 (0.00%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis atopic (Visit 1 to Visit 5)			
subjects affected / exposed	4 / 5359 (0.07%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis contact			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis diaper			

subjects affected / exposed	3 / 5359 (0.06%)	7 / 5349 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	4 / 5359 (0.07%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petechiae			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	3 / 5359 (0.06%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	5 / 5359 (0.09%)	6 / 5349 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria chronic			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria papular			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hematuria			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyuria			
subjects affected / exposed	6 / 5359 (0.11%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stag horn calculus			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vesicoureteric reflux			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle twitching			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigger finger			
subjects affected / exposed	3 / 5359 (0.06%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Gastroenteritis (Visit 5 to Visit 6) subjects affected / exposed ^[11]	3 / 4359 (0.07%)	2 / 4328 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract (Visit 5 to Visit 6)			
subjects affected / exposed ^[12]	0 / 4359 (0.00%)	3 / 4328 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed ^[13]	0 / 4359 (0.00%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kawasaki's disease (Visit 5 to Visit 6)			
subjects affected / exposed ^[14]	1 / 4359 (0.02%)	0 / 4328 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	3 / 5359 (0.06%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	3 / 5359 (0.06%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acarodermatitis			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			

subjects affected / exposed	5 / 5359 (0.09%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
subjects affected / exposed	10 / 5359 (0.19%)	7 / 5349 (0.13%)	
occurrences causally related to treatment / all	0 / 10	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoviral conjunctivitis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoviral upper respiratory infection			
subjects affected / exposed	0 / 5359 (0.00%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal cellulitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteremia			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteriuria			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	171 / 5359 (3.19%)	186 / 5349 (3.48%)	
occurrences causally related to treatment / all	0 / 171	0 / 186	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	36 / 5359 (0.67%)	41 / 5349 (0.77%)	
occurrences causally related to treatment / all	0 / 36	0 / 41	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			
subjects affected / exposed	0 / 5359 (0.00%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	23 / 5359 (0.43%)	15 / 5349 (0.28%)	
occurrences causally related to treatment / all	0 / 23	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter intestinal infection			

subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	3 / 5359 (0.06%)	10 / 5349 (0.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis of male external genital organ			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis orbital			
subjects affected / exposed	2 / 5359 (0.04%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall abscess			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chlamydial infection			
subjects affected / exposed	2 / 5359 (0.04%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis bacterial			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis infective			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis viral			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious (Visit 1 to Visit 5)			
subjects affected / exposed	30 / 5359 (0.56%)	29 / 5349 (0.54%)	
occurrences causally related to treatment / all	0 / 30	0 / 29	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 5359 (0.11%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema infected			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis brain stem			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			

subjects affected / exposed	5 / 5359 (0.09%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottitis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-barr virus infection			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	35 / 5359 (0.65%)	40 / 5349 (0.75%)	
occurrences causally related to treatment / all	0 / 35	0 / 40	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	37 / 5359 (0.69%)	53 / 5349 (0.99%)	
occurrences causally related to treatment / all	0 / 37	0 / 53	
deaths causally related to treatment / all	0 / 0	0 / 0	
External ear cellulitis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye abscess			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Folliculitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis viral			

subjects affected / exposed	14 / 5359 (0.26%)	20 / 5349 (0.37%)	
occurrences causally related to treatment / all	0 / 14	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis (Visit 1 to Visit 5)			
subjects affected / exposed	136 / 5359 (2.54%)	178 / 5349 (3.33%)	
occurrences causally related to treatment / all	0 / 136	0 / 178	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	3 / 5359 (0.06%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis caliciviral			
subjects affected / exposed	6 / 5359 (0.11%)	7 / 5349 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis escherichia coli			
subjects affected / exposed	0 / 5359 (0.00%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norwalk virus			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	9 / 5359 (0.17%)	44 / 5349 (0.82%)	
occurrences causally related to treatment / all	0 / 9	0 / 44	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	27 / 5359 (0.50%)	36 / 5349 (0.67%)	
occurrences causally related to treatment / all	0 / 27	0 / 36	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis shigella			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	18 / 5359 (0.34%)	20 / 5349 (0.37%)	
occurrences causally related to treatment / all	0 / 18	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematoma			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematoma infection			
subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus infection			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus sepsis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	17 / 5359 (0.32%)	16 / 5349 (0.30%)	
occurrences causally related to treatment / all	0 / 17	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			
subjects affected / exposed	28 / 5359 (0.52%)	16 / 5349 (0.30%)	
occurrences causally related to treatment / all	0 / 28	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impetigo			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected sebaceous cyst			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	10 / 5359 (0.19%)	21 / 5349 (0.39%)	
occurrences causally related to treatment / all	0 / 10	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kawasaki's disease (Visit 1 to Visit 5)			
subjects affected / exposed	13 / 5359 (0.24%)	9 / 5349 (0.17%)	
occurrences causally related to treatment / all	0 / 13	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteremia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	2 / 5359 (0.04%)	6 / 5349 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localized infection			

subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	8 / 5359 (0.15%)	9 / 5349 (0.17%)	
occurrences causally related to treatment / all	0 / 8	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis (Visit 1 to Visit 5)			
subjects affected / exposed	2 / 5359 (0.04%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis bacterial			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Measles			
subjects affected / exposed	3 / 5359 (0.06%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinal abscess			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	2 / 5359 (0.04%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myringitis bullous			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal vestibulitis			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	6 / 5359 (0.11%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	11 / 5359 (0.21%)	17 / 5349 (0.32%)	
occurrences causally related to treatment / all	0 / 11	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			

subjects affected / exposed	19 / 5359 (0.35%)	14 / 5349 (0.26%)	
occurrences causally related to treatment / all	0 / 19	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae viral laryngotracheobronchitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	3 / 5359 (0.06%)	11 / 5349 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perianal abscess			
subjects affected / exposed	2 / 5359 (0.04%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			

subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	32 / 5359 (0.60%)	30 / 5349 (0.56%)	
occurrences causally related to treatment / all	0 / 32	0 / 30	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal infection			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	27 / 5359 (0.50%)	42 / 5349 (0.79%)	
occurrences causally related to treatment / all	0 / 27	0 / 42	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia adenoviral (non-fatal SAE)			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia haemophilus			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	9 / 5359 (0.17%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 5359 (0.04%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	1 / 5359 (0.02%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyomyositis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	42 / 5359 (0.78%)	53 / 5349 (0.99%)	
occurrences causally related to treatment / all	0 / 42	0 / 53	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	5 / 5359 (0.09%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 5359 (0.06%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Roseola			
subjects affected / exposed	8 / 5359 (0.15%)	5 / 5349 (0.09%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scarlet fever			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	1 / 5359 (0.02%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	4 / 5359 (0.07%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal scalded skin syndrome			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	4 / 5359 (0.07%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	6 / 5359 (0.11%)	3 / 5349 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis bacterial			

subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	126 / 5359 (2.35%)	171 / 5349 (3.20%)	
occurrences causally related to treatment / all	0 / 126	0 / 171	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection (Visit 1 to Visit 5)			
subjects affected / exposed	28 / 5359 (0.52%)	38 / 5349 (0.71%)	
occurrences causally related to treatment / all	0 / 28	0 / 38	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	3 / 5359 (0.06%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	34 / 5359 (0.63%)	31 / 5349 (0.58%)	
occurrences causally related to treatment / all	0 / 34	0 / 31	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral myocarditis			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pharyngitis			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			

subjects affected / exposed	13 / 5359 (0.24%)	16 / 5349 (0.30%)	
occurrences causally related to treatment / all	0 / 13	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral tonsillitis			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	25 / 5359 (0.47%)	31 / 5349 (0.58%)	
occurrences causally related to treatment / all	0 / 25	0 / 31	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia adenoviral (fatal SAE)	Additional description: This reported SAE is a fatal SAE.		
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration (Visit 5 to Visit 6)			
subjects affected / exposed ^[15]	0 / 4359 (0.00%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia (Visit 5 to Visit 6)			
subjects affected / exposed ^[16]	0 / 4359 (0.00%)	1 / 4328 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorexia			
subjects affected / exposed	4 / 5359 (0.07%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	6 / 5359 (0.11%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration (Visit 1 to Visit 5)			

subjects affected / exposed	1 / 5359 (0.02%)	4 / 5349 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	2 / 5359 (0.04%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding disorder of infancy or early childhood			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycemia (Visit 1 to Visit 5)			
subjects affected / exposed	0 / 5359 (0.00%)	2 / 5349 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycemic seizure			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalemia			
subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatremia			
subjects affected / exposed	1 / 5359 (0.02%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolemia			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			

subjects affected / exposed	1 / 5359 (0.02%)	0 / 5349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic disorder (non-fatal SAE)			
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight gain poor			
subjects affected / exposed	2 / 5359 (0.04%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic disorder (fatal SAE)	Additional description: This reported SAE is a fatal SAE.		
subjects affected / exposed	0 / 5359 (0.00%)	1 / 5349 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the

study up to Visit 5.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This serious adverse event was reported for the time period from Visit 5 to Visit 6. The number of subjects who entered the study at Visit 5 was less than those who started and completed the study up to Visit 5.

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Rotarix Group	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 5359 (0.00%)	0 / 5349 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 June 2003	Rationale: Evaluated the safety of GSK Biologicals' HRV vaccine, administration of OPV will be deferred from the study vaccine administration by minimum 2 weeks. (1, 2) Interim analysis of an ongoing study (rota-021) in Latin America did not establish the non-inferiority of the all-in-one formulation planned to be used in study 023 as compared to the initial formulation. The initial formulation was therefore used instead of all-in-one formulation.
24 February 2004	Unlike planned, Malaysia and Thailand did not participate in this study, for logistical and internal organizational reasons. This led to reduction of the sample size. The power was recalculated for the reduced sample size. Because of the overall reduction in sample size, it was decided that all subjects will be followed for efficacy and safety until they reach 2 years of age, instead of only a subset. The method for power computation for the primary safety objective and the statistical analysis section on safety was adapted to reflect a recommendation from the statistician from the IDMC. An exclusion criterion was added to exclude infants who could have rare underlying congenital abnormalities caused by consanguinity.
26 April 2005	An interim analysis on the safety and immunogenicity data was performed in June 2005. Unblinding at the level of individual data was restricted to the Statistician and database administration until the study end. An interim study report was written for this time point.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported