Clinical trial results:
A Phase III, randomized, observer-blind, controlled, multi-center clinical study to evaluate the efficacy, safety and immunogenicity of one and two intramuscular doses of FLUAD® versus control vaccines in unprimed healthy subjects aged 6 to <72 months.

Summary

EudraCT number	2007-003786-41
Trial protocol	DE FI IT HU BE
Global end of trial date	05 August 2010

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	21 December 2014
Version creation reason	• Correction of full data set re-QC study because of EudraCT system glitch and possible updates to results required.

Trial information

Trial identification

Sponsor protocol code	V70P5

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00644059
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	Novartis Vaccines, Via Fiorentina, 1., Siena., Italy, 53100.
Public contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000149-PIP01-07
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	03 November 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 August 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the safety and tolerability of one or two 0.25mL IM doses of FLUAD in unprimed children aged 6 to <36 months, compared with Agrippal S1 and/or with Influsplit SSW (flu vaccine control), in terms of any solicited local and systemic reactions (combined) reported within 7 days after any vaccination.
To demonstrate protection provided by two 0.25mL intramuscular (IM) doses of Fluad (TIV-adj) in unprimed children aged 6 to <36 months, compared with Menjugate/ Encepur Children (Non-flu vaccine control), against influenza illness caused by virus-confirmed community-acquired influenza wild type strains matching with those contained in the vaccine.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine were available in case of any anaphylactic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 2083
Country: Number of subjects enrolled	Italy: 61
Country: Number of subjects enrolled	Germany: 2758
Worldwide total number of subjects	4902
EEA total number of subjects	4902

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2046
Children (2-11 years)	2856
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:

In season 2007/08: 28 active sites in Germany;
In season 2008/09: 83 active sites+ 1 coordinating site in Germany, 15 sites in Finland;
In season 2009/10: 15 sites in Finland, 2 sites in Italy.

Pre-assignment

Screening details:

All subjects enrolled were included in the trial. The data entered is for the overall study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TIV-adj

Arm description:

Subjects aged 6 to < 36 months received 0.25 mL and those aged 36 to <72 months received 0.5 mL of each injection of adjuvanted trivalent inactivated subunit influenza vaccine

Arm type	Experimental
Investigational medicinal product name	Adjuvanted Trivalent influenza vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.25mL in children aged 6 to<36 months; 2 doses of 0.5mL in children aged 36 to<72 months given intramuscularly in the non-dominant arm, or in the thigh, depending on age.

Arm title	Flu-control

Arm description:

Subjects aged 6 to < 36 months received 0.25 mL and those aged 36 to <72 months received 0.5 mL of each injection of Non-adjuvanted trivalent inactivated subunit influenza vaccine or non-adjuvanted trivalent inactivated split influenza vaccine.

Arm type	Active comparator
Investigational medicinal product name	Influsplit SSW
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

A 0.25 mL pre-filled syringe pediatric dose is provided for subject aged 6 to <36 months and a 0.5 mL pre-filled syringe is provided for subject aged 36 to <72 months.

Investigational medicinal product name	Non adjuvanted Trivalent influenza vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.25mL (children aged 6 to<36 months) or 0.5mL children aged 36 to<72 months) given intramuscularly in the non-dominant arm, or in the thigh, depending on age.

Arm title	Non-flu Control

Arm description:

Subjects aged 6 to <12 months received 2 doses of 0.5 mL of Novartis Menningocoocal C conjugate vaccine and subjects aged 12 to <72 months received 2 doses of 0.25 mL of Tick-borne encephalitis (TBE) vaccine

Arm type	Active comparator
Investigational medicinal product name	Men C vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe, Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

MenC Vaccine: 2 doses of 0.5mL in subjects aged 6 to <12 months;
TBE Vacine: Children 2 doses of 0.25mL in subjects aged 12 to <72 months given intramuscularly in the non-dominant arm, or in the thigh, depending on age.

Investigational medicinal product name	Encepur
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.25mL was injected in subjects aged 12 to <72 months.

Number of subjects in period 1	TIV-adj	Flu-control	Non-flu Control
Started	2019	1849	1034
Completed	1895	1726	969
Not completed	124	123	65
Inapproopriate enrollment	1	-	-
Consent withdrawn by subject	52	60	30
Inappropriate enrollment	-	3	-
Unable to classify	6	2	3
Adverse event	8	5	1
Lost to follow-up	37	34	16
Protocol deviation	20	19	15

Baseline characteristics

Reporting groups	
Reporting group title	TIV-adj
Reporting group description:	
Subjects aged 6 to < 36 months received 0.25 mL and those aged 36 to <72 months received 0.5 mL of each injection of adjuvanted trivalent inactivated subunit influenza vaccine	
Reporting group title	Flu-control
Reporting group description:	
Subjects aged 6 to < 36 months received 0.25 mL and those aged 36 to <72 months received 0.5 mL of each injection of Non-adjuvanted trivalent inactivated subunit influenza vaccine or non-adjuvanted trivalent inactivated split influenza vaccine.	
Reporting group title	Non-flu Control
Reporting group description:	
Subjects aged 6 to <12 months received 2 doses of 0.5 mL of Novartis Menningocoocal C conjugate vaccine and subjects aged 12 to <72 months received 2 doses of 0.25 mL of Tick-borne encephalitis (TBE) vaccine	

Reporting group values	TIV-adj	Flu-control	Non-flu Control
Number of subjects	2019	1849	1034
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: months			
arithmetic mean	31.9	32.6	32.2
standard deviation	± 19.8	± 20.1	± 19.8
Gender categorical Units: Subjects			
Female	962	903	484
Male	1057	946	550

Reporting group values	Total		
Number of subjects	4902		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	2349		
Male	2553		

End points

End points reporting groups

Reporting group title	TIV-adj
Reporting group description:	
Subjects aged 6 to < 36 months received 0.25 mL and those aged 36 to <72 months received 0.5 mL of each injection of adjuvanted trivalent inactivated subunit influenza vaccine	
Reporting group title	Flu-control
Reporting group description:	
Subjects aged 6 to < 36 months received 0.25 mL and those aged 36 to <72 months received 0.5 mL of each injection of Non-adjuvanted trivalent inactivated subunit influenza vaccine or non-adjuvanted trivalent inactivated split influenza vaccine.	
Reporting group title	Non-flu Control
Reporting group description:	
Subjects aged 6 to <12 months received 2 doses of 0.5 mL of Novartis Menningocoocal C conjugate vaccine and subjects aged 12 to <72 months received 2 doses of 0.25 mL of Tick-borne encephalitis (TBE) vaccine	
Subject analysis set title	TIV-adj (6 to <36 Months)-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the exposed population who provided post-baseline safety data	
Subject analysis set title	Flu-control (6 to <36 Months)-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the exposed population who provided post-baseline safety data.	
Subject analysis set title	Flu-control (36 to <72 Months)-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the enrolled population who provided post-baseline safety data.	
Subject analysis set title	TIV-adj (36 to <72 Months)-safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the enrolled population who provided post-baseline safety data.	
Subject analysis set title	Non-flu control (TBE/Men C Vaccine)-Safety
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the exposed population who provided post-baseline safety data.	
Subject analysis set title	Non-Flu-control (36 to <72 Months)-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the enrolled population who provided post-baseline safety data.	
Subject analysis set title	Non-Flu control (6 to < 72 Months)-safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the enrolled population who provided post-baseline safety data.	
Subject analysis set title	Flu-control (6 to <72 Months)-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the enrolled population who provided post-baseline safety data.	
Subject analysis set title	TIV-adj (6 to <72 Months)-Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the enrolled population who provided post-baseline safety data.

Subject analysis set title	Flu Control (6 to <36 Months)-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled set who received study vaccination.

Subject analysis set title	Non-flu Control (6 to <36 Months)-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled set who received study vaccination.

Subject analysis set title	TIV-adj (36 to <72 Months)-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled populatio who received study vaccination.

Subject analysis set title	TIV-adj (6 to < 36 Months)-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled set who received study vaccination.

Subject analysis set title	Non-flu control (36 to <72 Months)- FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled populatio who received study vaccination.

Subject analysis set title	Flu control (36 to <72 Months)- FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled populatio who received study vaccination.

Subject analysis set title	TIV-adj-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled set who received study vaccination.

Subject analysis set title	Flu- control-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled set who received study vaccination.

Subject analysis set title	Non-flu control-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled set who received study vaccination.

Primary: 1. Number of Subjects (Unprimed) 6 to <36 Months Age With Local and Systemic Reactions After Any Vaccination for All Seasons, Comparison of Adjuvanted Trivalent Influenza Vaccine (aTIV) and Flu Vaccine Control.

End point title	1. Number of Subjects (Unprimed) 6 to <36 Months Age With Local and Systemic Reactions After Any Vaccination for All Seasons, Comparison of Adjuvanted Trivalent Influenza Vaccine (aTIV) and Flu Vaccine Control.[1]

End point description:

Safety was assessed as the number of subjects who reported solicited local or systemic adverse events after any vaccination with TIV-adj for all seasons.

End point type	Primary

End point timeframe:

7 days post-vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	TIV-adj (6 to <36 Months)-Safety	Flu-control (6 to <36 Months)-Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1178	1068		
Units: Number of subjects				
number (not applicable)				
Any Local	625	481		
Injection Site Ecchymosis	147	103		
Injection Site Erythema	423	322		
Injection Site Induration	214	131		
Swelling	123	89		
Tender. at inj.site	330	246		
Any Systemic	785	694		
Change in eat. hab.	325	261		
Sleepiness	380	312		
Unusual crying	386	345		
Irritability	387	353		
Vomiting	131	118		
Diarrhea	258	211		
Shivering	77	69		
Any Other	358	317		
Fever (38-38.9°C) (N=1177,1068)	169	143		
Fever (39-39.9°C) (N=1177,1068)	61	43		
Fever (>40.0°C) (N=1177,1068)	3	3		
Analg.Antipyr.Used (N=1176,1068)	358	317		

Statistical analyses

No statistical analyses for this end point

Primary: 2. Percentage of Subjects (Unprimed) Aged 6 to <36 Months With Virus-Confirmed Influenza, Comparison of Adjuvanted Trivalent Influenza Vaccine and Non-Flu Control (Men C/TBE vaccine)

End point title	2. Percentage of Subjects (Unprimed) Aged 6 to <36 Months With Virus-Confirmed Influenza, Comparison of Adjuvanted Trivalent Influenza Vaccine and Non-Flu Control (Men C/TBE vaccine)

End point description:

Virus-confirmed influenza illnesses were assessed and compared between the adjuvanted influenza vaccine (TIV-adj) and non-influenza vaccines (Non-flu control) in 6 to <36 month unprimed subjects for Absolute Efficacy. This primary endpoint is only for homologous strains.

End point type	Primary

End point timeframe:

3 weeks after 2nd vaccination

End point values	Non-flu Control (6 to <36 Months)-FAS	TIV-adj (6 to < 36 Months)-FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	469	916		
Units: Percentage of subjects				
number (not applicable)				
Season 2007/2008; N=187, 97	0	0		
Season 2008/2009	4.05	0.76		

Statistical analyses

Statistical analysis title	Comparison of aTIV and Non-flu vaccine control

Statistical analysis description:

Absolute vaccine efficacy (VE) was calculated as (1- the relative risk)100%. Relative Risk for virus-confirmed symptomatic influenza illness in the TIV-adj group vs. the non-flu control group. VE denotes the vaccine efficacy, i.e. 1-Itest/Inon-flu ctrl, where I stands for the population average incidence of influenza.
Absolute efficacy of TIV-adj is at most 40% (i.e. the probability of an influenza in the test group relative to that in the non-flu vaccine group is at least 0.6)

Comparison groups	TIV-adj (6 to < 36 Months)-FAS v Non-flu Control (6 to <36 Months)-FAS
Number of subjects included in analysis	1385
Analysis specification	Pre-specified
Analysis type	other
Method	Poisson Regression Model
Parameter estimate	Vaccine Efficacy
Point estimate	81.36
Confidence interval	
level	Other: 97.66 %
sides	2-sided
lower limit	49.24
upper limit	93.16

Secondary: 3. Number of Subjects (Unprimed) of 6 to <72 Months Age With Local and Systemic Reactions After Any Vaccination

End point title	3. Number of Subjects (Unprimed) of 6 to <72 Months Age With Local and Systemic Reactions After Any Vaccination

End point description:

Safety was assessed as the number of subjects aged 6 to <72 months who reported solicited local or systemic adverse events after any vaccination with TIV-adj for all seasons.

End point type	Secondary

End point timeframe:

7 days post-vaccination

End point values	TIV-adj (6 to <36 Months)-Safety	Flu-control (6 to <36 Months)-Safety	Flu-control (36 to <72 Months)-Safety	TIV-adj (36 to <72 Months)-safety
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1178	1068	778	833
Units: Number of Subjects				
number (not applicable)				
Any Local	625	481	466	569
Inj. site ecchymosis(N=1178,833,1068,777,607,	147	103	93	130
Inj. site erythema(N=1178,833,1068,777,607,4	423	322	269	320
Inj. site induration(N=1178,833,1068,777,607,4	214	131	152	168
Inj. site swelling(N=1178,833,1068,777,607,422	123	89	128	155
Inj. site tenderness(N=1178,0,1068,0,607,0)	330	246	0	0
Inj. site pain(N=0,833,0,777,0,422)	0	0	360	477
Any Systemic	785	694	341	523
Change in eating habits(N=1178,0,1068,0,607,0)	325	261	0	0
Sleepiness(N=1178,0,1068,0,607,0)	380	312	0	0
Unusual crying(N=1178,0,1068,0,607,0)	386	345	0	0
Irritability(N=1178,0,1068,0,607,0)	387	353	0	0
Vomiting(N=1178,0,1068,0,607,0)	131	118	0	0
Diarrhea(N=1178,0,1068,0,607,0)	258	211	0	0
Shivering(N=1178,0,1068,0,607,0)	77	69	0	0
Chills shivering(N=0,833,0,777,0,422)	0	0	51	130
Malaise(N=0,833,0,777,0,422)	0	0	118	196
Myalgia(N=0,833,0,777,0,422)	0	0	100	183
Arthralgia(N=0,833,0,777,0,422)	0	0	37	82
Headache(N=0,833,0,777,0,422)	0	0	100	197
Sweating(N=0,833,0,777,0,422)	0	0	42	69
Fatigue(N=0,833,0,777,0,422)	0	0	222	337
Any Other	358	317	94	196
Fever(38-38.9C)(N=1177,833,1068,775,607,421)	169	143	55	133
Fever(39-39.9C)(N=1177,833,1068,775,607,421)	61	43	17	50
Fever(≥40.0C)(N=1177,833,1068,775,607,421)	3	3	2	1
Analg.Antipyr.Used(N=1176,833,1068,777,607,422)	358	317	94	196

End point values	Non-flu control (TBE/Men C Vaccine)-Safety	Non-Flu-control (36 to <72 Months)-Safety		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	422		
Units: Number of Subjects				
number (not applicable)				
Any Local	315	232		
Inj. site ecchymosis(N=1178,833,1068,777,607,	69	49		
Inj. site erythema(N=1178,833,1068,777,607,4	239	129		
Inj. site induration(N=1178,833,1068,777,607,4	153	80		
Inj. site swelling(N=1178,833,1068,777,607,422	82	55		
Inj. site tenderness(N=1178,0,1068,0,607,0)	171	0		
Inj. site pain(N=0,833,0,777,0,422)	0	180		
Any Systemic	370	211		
Change in eating habits(N=1178,0,1068,0,607,0)	162	0		
Sleepiness(N=1178,0,1068,0,607,0)	186	0		
Unusual crying(N=1178,0,1068,0,607,0)	175	0		
Irritability(N=1178,0,1068,0,607,0)	187	0		
Vomiting(N=1178,0,1068,0,607,0)	66	0		
Diarrhea(N=1178,0,1068,0,607,0)	114	0		
Shivering(N=1178,0,1068,0,607,0)	50	0		
Chills shivering(N=0,833,0,777,0,422)	0	37		
Malaise(N=0,833,0,777,0,422)	0	63		
Myalgia(N=0,833,0,777,0,422)	0	66		
Arthralgia(N=0,833,0,777,0,422)	0	27		
Headache(N=0,833,0,777,0,422)	0	54		
Sweating(N=0,833,0,777,0,422)	0	31		
Fatigue(N=0,833,0,777,0,422)	0	123		
Any Other	159	69		
Fever(38-38.9C)(N=1177,833,1068,775,607,421)	62	37		
Fever(39-39.9C)(N=1177,833,1068,775,607,421)	34	19		
Fever(≥40.0C)(N=1177,833,1068,775,607,421)	2	1		
Analg.Antipyr.Used(N=1176,833,1068,777,607,422)	159	69		

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Number of Subjects (Unprimed) With Unsolicited Adverse Events Reported After Any Vaccination

End point title	4. Number of Subjects (Unprimed) With Unsolicited Adverse Events Reported After Any Vaccination

End point description:

Number of subjects aged 6 to <36 months and in the overall age cohort (unprimed children aged 6 to <72 months) experiencing each of the unsolicited adverse events throughout the study.

End point type	Secondary

End point timeframe:

Day 1 to Day 181

End point values	TIV-adj (6 to <36 Months)-Safety	Flu-control (6 to <36 Months)-Safety	Non-flu control (TBE/Men C Vaccine)-Safety	Non-Flu control (6 to < 72 Months)-safety
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1177	1069	607	1029
Units: Number of subjects				
number (not applicable)				
Any AEs	1045	938	530	867
At least possibly related AEs	152	124	90	137
Serious AEs	91	104	65	110
At least possibly related SAEs	1	1	3	3
AEs leading to discontinuation	6	9	1	1

End point values	Flu-control (6 to <72 Months)-Safety	TIV-adj (6 to <72 Months)-Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1846	2012		
Units: Number of subjects				
number (not applicable)				
Any AEs	1566	1714		
At least possibly related AEs	203	262		
Serious AEs	169	122		
At least possibly related SAEs	2	2		
AEs leading to discontinuation	10	9		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Percentage of Subjects (Unprimed) Aged 6 to <72 Months With Virus-Confirmed Influenza, Comparison of aTIV to Non-flu Vaccine Control and Flu-vaccine Control (Matched Strains)

End point title	5. Percentage of Subjects (Unprimed) Aged 6 to <72 Months With Virus-Confirmed Influenza, Comparison of aTIV to Non-flu Vaccine Control and Flu-vaccine Control (Matched Strains)

End point description:

Virus-confirmed influenza illnesses were assessed and compared between the adjuvanted influenza vaccine (TIV-adj) and non-influenza vaccines (Non-flu control) in subjects aged 6 to <72 months (unprimed) for Absolute Efficacy.
For Relative efficacy, the comparison was made between adjuvanted influenza vaccine (TIV-adj) and flu vaccine control.

End point type	Secondary
End point timeframe: 3 weeks after 2nd vaccination	

End point values	Flu Control (6 to <36 Months)-FAS	Non-flu Control (6 to <36 Months)-FAS	TIV-adj (36 to <72 Months)-FAS	TIV-adj (6 to < 36 Months)-FAS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	902	469	698	916
Units: Percentage of subjects				
number (not applicable)				
Matched strain(Season2007/08)N=187,97,93,13	0	0	0	0
Matched strain (Season2008/09)	2.44	4.05	0.29	0.76

End point values	Non-flu control (36 to <72 Months)- FAS	Flu control (36 to <72 Months)- FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	360	706		
Units: Percentage of subjects				
number (not applicable)				
Matched strain(Season2007/08)N=187,97,93,13	0	0		
Matched strain (Season2008/09)	6.11	3.12		

Statistical analyses

Statistical analysis title	Comparison of aTIV to Non-flu and flu controls

Statistical analysis description:

Absolute vaccine efficacy (VE) was calculated as (1- the relative risk)100%. Relative Risk for virus-confirmed symptomatic influenza illness in the TIV-adj group vs. the non-flu control group. VE denotes the vaccine efficacy, i.e. 1-Itest/Inon-flu ctrl, where I stands for the incidence of influenza.

Absolute efficacy of TIV-adj is at most 40% (i.e. the probability of an influenza in the test group relative to that in the non-flu vaccine group is at least 0.6)

Comparison groups	TIV-adj (36 to <72 Months)-FAS v Non-flu control (36 to <72 Months)- FAS
Number of subjects included in analysis	1058
Analysis specification	Pre-specified
Analysis type	other
Method	[Poisson Regression Model]
Parameter estimate	Vaccine Efficacy
Point estimate	95.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	80.92
upper limit	98.94

Statistical analysis title	Comparison of aTIV to Non-Flu and Flu controls

Statistical analysis description:

Absolute vaccine efficacy (VE) was calculated as (1- the relative risk)100%. Relative Risk for virus-confirmed symptomatic influenza illness in the TIV-adj group vs. the non-flu control group. VE denotes the vaccine efficacy, i.e. 1-Itest/Inon-flu ctrl, where I stands for the incidence of influenza.

Absolute efficacy of TIV-adj is at most 40% (i.e. the probability of an influenza in the test group relative to that in the non-flu vaccine group is at least 0.6)

Comparison groups	TIV-adj (6 to < 36 Months)-FAS v Non-flu Control (6 to <36 Months)-FAS
Number of subjects included in analysis	1385
Analysis specification	Pre-specified
Analysis type	other
Method	Poisson Regression Model
Parameter estimate	Vaccine Efficacy
Point estimate	81.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	49.24
upper limit	93.16

Statistical analysis title	Comparison of aTIV to Non-flu and flu controls

Statistical analysis description:

Relative efficacy for TIV-adj was to be calculated as VE = (1-Itest/Ictrl)100%, where I is the incidence of influenza, i.e. percentage of subjects with virus-confirmed symptomatic influenza A or B illness, in the investigational agent (TIV-adj) group or in the flu vaccine control group.

Comparison groups	TIV-adj (6 to < 36 Months)-FAS v Flu Control (6 to <36 Months)-FAS
Number of subjects included in analysis	1818
Analysis specification	Pre-specified
Analysis type	other
Method	Mantel-Haenszel
Parameter estimate	Vaccine Efficacy
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.73

Statistical analysis title	Comparison of aTIV to Non-flu and Flu controls

Statistical analysis description:

Relative efficacy for TIV-adj was to be calculated as VE = (1-Itest/Ictrl)100%, where I is the incidence of influenza, i.e. percentage of subjects with virus-confirmed symptomatic influenza A or B illness, in the investigational agent (TIV-adj) group or in the flu vaccine control group.

Comparison groups	TIV-adj (36 to <72 Months)-FAS v Flu control (36 to <72 Months)- FAS
Number of subjects included in analysis	1404
Analysis specification	Pre-specified
Analysis type	other
Method	Mantel-Haenszel
Parameter estimate	Vaccine Efficacy]
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.38

Secondary: 6. Percentage of Subjects (Unprimed) Aged 6 to <72 Months With Virus-Confirmed Influenza, Comparison of aTIV to Non-flu Vaccine Control and Flu Vaccine Control (Any Strains)

End point title	6. Percentage of Subjects (Unprimed) Aged 6 to <72 Months With Virus-Confirmed Influenza, Comparison of aTIV to Non-flu Vaccine Control and Flu Vaccine Control (Any Strains)

End point description:

Virus-confirmed influenza illnesses (regardless of antigenic match to those contained in the vaccine) were assessed and compared between the adjuvanted influenza vaccine (TIV-adj) and non-influenza vaccines (Non-flu control) in subjects aged 6 to <72 months (unprimed) for Absolute Efficacy.

For Relative efficacy, the comparison was made between adjuvanted influenza vaccine (TIV-adj) and flu vaccine control.

End point type	Secondary

End point timeframe:

3 weeks after 2nd vaccination

End point values	Flu Control (6 to <36 Months)-FAS	Non-flu Control (6 to <36 Months)-FAS	TIV-adj (36 to <72 Months)-FAS	TIV-adj (6 to < 36 Months)-FAS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	902	469	698	916
Units: Percentage of subjects				
number (not applicable)				
Any Strain (Season 2007/08)N=187,97,93,136,67,71	0	2.06	0.74	0
Any Strain (Season 2008/09)	2.77	4.26	0.43	0.98

End point values	Non-flu control (36 to <72 Months)- FAS	Flu control (36 to <72 Months)- FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	360	706		
Units: Percentage of subjects				
number (not applicable)				
Any Strain (Season 2007/08)N=187,97,93,136,67,71	2.99	0		
Any Strain (Season 2008/09)	6.39	3.54		

Statistical analyses

Statistical analysis title	Comparison of aTIV to Non-flu and Flu controls

Statistical analysis description:

Absolute vaccine efficacy (VE) was calculated as (1- the relative risk)100%. Relative Risk for virus-confirmed symptomatic influenza illness in the TIV-adj group vs. the non-flu control group. VE denotes the vaccine efficacy, i.e. 1-Itest/Inon-flu ctrl, where I stands for the incidence of influenza. Absolute efficacy of TIV-adj is at most 40% (i.e. the probability of an influenza in the test group relative to that in the non-flu vaccine group is at least 0.6).

Comparison groups	TIV-adj (36 to <72 Months)-FAS v Non-flu control (36 to <72 Months)- FAS
Number of subjects included in analysis	1058
Analysis specification	Pre-specified
Analysis type	other
Method	Poisson Regression Model
Parameter estimate	Vaccine Efficacy
Point estimate	92.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	77.35
upper limit	97.24

Statistical analysis title	Comparison of aTIV to Non-flu and Flu controls

Statistical analysis description:

Relative efficacy for TIV-adj was to be calculated as VE = (1-Itest/Ictrl)100%, where I is the incidence of influenza, i.e. percentage of subjects with virus-confirmed symptomatic influenza A or B illness, in the investigational agent (TIV-adj) group or in the flu vaccine control group.

Comparison groups	TIV-adj (6 to < 36 Months)-FAS v Flu Control (6 to <36 Months)-FAS
Number of subjects included in analysis	1818
Analysis specification	Pre-specified
Analysis type	other
Method	Poisson Regression Model
Parameter estimate	Vaccine Efficacy
Point estimate	64.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	23.21
upper limit	83.28

Statistical analysis title	Comparison of aTIV to Non-flu and Flu controls

Statistical analysis description:

Absolute vaccine efficacy (VE) was calculated as (1- the relative risk)100%. Relative Risk for virus-confirmed symptomatic influenza illness in the TIV-adj group vs. the non-flu control group. VE denotes the vaccine efficacy, i.e. 1-Itest/Inon-flu ctrl, where I stands for the population average incidence of influenza.
Absolute efficacy of TIV-adj is at most 40% (i.e. the probability of an influenza in the test group relative to that in the non-flu vaccine group is at least 0.6)

Comparison groups	TIV-adj (6 to < 36 Months)-FAS v Non-flu Control (6 to <36 Months)-FAS
Number of subjects included in analysis	1385
Analysis specification	Pre-specified
Analysis type	other
Method	Poisson Regression Model
Parameter estimate	Vaccine Efficacy
Point estimate	79.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	54.78
upper limit	90.42

Statistical analysis title	Comparison of aTIV to Non-flu and Flu controls

Statistical analysis description:

Relative efficacy for TIV-adj was to be calculated as VE = (1-Itest/Ictrl)100%, where I is the incidence of influenza, i.e. percentage of subjects with virus-confirmed symptomatic influenza A or B illness, in the investigational agent (TIV-adj) group or in the flu vaccine control group.

Comparison groups	TIV-adj (36 to <72 Months)-FAS v Flu control (36 to <72 Months)- FAS
Number of subjects included in analysis	1404
Analysis specification	Pre-specified
Analysis type	other
Method	Poisson Regression Model
Parameter estimate	Vaccine Efficacy
Point estimate	85.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.95
upper limit	94.99

Secondary: 7. Number of Subjects (Unprimed) With Influenza Like Illnesses (ILIs) in the 6 to <72 Months Age Cohort for Combined Seasons 2007/08 and 2008/09

End point title	7. Number of Subjects (Unprimed) With Influenza Like Illnesses (ILIs) in the 6 to <72 Months Age Cohort for Combined Seasons 2007/08 and 2008/09

End point description:

Virus-confirmed influenza illnesses were assessed and trivalent adjuvanted influenza vaccine (TIV-adj) was compared with Non-flu control vaccine and Flu-control vaccine in 6 to <72 month old subjects for Influenza like illnesses for seasons 2007/08 and 2008/09.

End point type	Secondary

End point timeframe:

3 weeks after 2nd vaccination

End point values	TIV-adj-FAS	Flu- control-FAS	Non-flu control-FAS	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	1937	1772	993	
Units: Number of subjects				
number (not applicable)				
Subjects with ILI	425	436	253	
Outpatient visits	290	293	174	
Inpatient visits	20	26	19	
Outcome (Recovered)	414	431	248	
Outcome (Alive with sequelae)	5	2	2	
Outcome (Lost to follow-up)	3	1	0	
Outcome (ILI persisting)	3	1	3	
Outcome (Not available)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Number of Subjects With Influenza Like Illnesses (ILIs) in the 6 to <36 Months and in Overall Age Cohort (Unprimed Subjects Aged 6 to <72 Months) for Combined Seasons 2007/08 and 2008/09.

End point title	8. Number of Subjects With Influenza Like Illnesses (ILIs) in the 6 to <36 Months and in Overall Age Cohort (Unprimed Subjects Aged 6 to <72 Months) for Combined Seasons 2007/08 and 2008/09.

End point description:

Virus-confirmed influenza illnesses were assessed and trivalent adjuvanted influenza vaccine (TIV-adj) was compared with Non-flu control vaccine and Flu-control vaccine for Influenza like illnesses for seasons 2007/08 and 2008/09.

End point type	Secondary

End point timeframe:

3 weeks after 2nd vaccination

End point values	Flu Control (6 to <36 Months)-FAS	Non-flu Control (6 to <36 Months)-FAS	TIV-adj (6 to < 36 Months)-FAS	TIV-adj-FAS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	995	566	1103	1937
Units: Number of subjects				
number (not applicable)				
Subjects with ILI	272	163	280	425
Outpatient visits	183	113	192	290
Inpatient visits	19	14	13	20
Outcome (Recovered)	267	159	269	414
Outcome (Alive with sequelae)	2	2	5	5
Outcome (Lost to follow-up)	1	0	3	3
Outcome (ILI persisting)	1	2	3	3
Outcome (Not available)	1	0	0	0

End point values	Flu- control-FAS	Non-flu control-FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1772	993		
Units: Number of subjects				
number (not applicable)				
Subjects with ILI	436	253		
Outpatient visits	293	174		
Inpatient visits	26	19		
Outcome (Recovered)	431	248		
Outcome (Alive with sequelae)	2	2		
Outcome (Lost to follow-up)	1	0		
Outcome (ILI persisting)	1	3		
Outcome (Not available)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Loss of Days of Usual Activity (Job, School, Day Care, Household/Family/Community Activities) Due to Influenza Like Illness (ILI) in Subjects in Aged 6 to <72 and 6 to <36 Months and in Direct Caregivers Living in the Household.

End point title	9. Loss of Days of Usual Activity (Job, School, Day Care, Household/Family/Community Activities) Due to Influenza Like Illness (ILI) in Subjects in Aged 6 to <72 and 6 to <36 Months and in Direct Caregivers Living in the Household.

End point description:

Virus-confirmed influenza illnesses were assessed and trivalent adjuvanted influenza vaccine (TIV-adj) was compared with Non-flu control vaccine and Flu-control vaccine for Influenza like illnesses for seasons 2007/08 and 2008/09.

End point type	Secondary

End point timeframe:

3 weeks after 2nd vaccination

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	425	436	253	
Units: Days				
arithmetic mean (standard deviation)				
Mean bed days (6 to <72 mths)(N=419,426,250)	1.9 (± 2.3)	1.9 (± 2.4)	2.3 (± 2.7)	
Mean bed days (6 to <36 mths)(N=274,263,160)	2 (± 2.5)	1.8 (± 2.4)	2.1 (± 2.4)	
Mean inactive days(6 to <72 mths)(N=417,427,249)	3.1 (± 3.3)	2.9 (± 3.7)	3.3 (± 3.5)	
Mean inactive days(6 to <36 mths)(N=273,264,160)	2.9 (± 3.3)	2.6 (± 3.3)	3 (± 3.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Number of Events of Influenza Like Illness for Combined Seasons 2007/08 and 2008/09.

End point title	10. Number of Events of Influenza Like Illness for Combined Seasons 2007/08 and 2008/09.

End point description:

The number of events of Influenza like Illness reported by subjects aged 6 to <72 months was assessed for combined seasons 2007/08 and 2008/09.

End point type	Secondary

End point timeframe:

3 weeks after 2nd vaccination

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	425	436	253	
Units: Events				
arithmetic mean (standard deviation)				
Mean ILI events (6 to <72 mths)(N=425,436,253)	1.2 (± 0.5)	1.2 (± 0.5)	1.3 (± 0.6)	
Mean ILI events (6 to <36 mths)(N=280,272,163)	1.3 (± 0.5)	1.3 (± 0.5)	1.3 (± 0.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of GMRs, in Unprimed Subjects Aged 6 to <36 Months or Season 2008/09 (Homologous and Heterologous Strains)

End point title	11. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of GMRs, in Unprimed Subjects Aged 6 to <36 Months or Season 2008/09 (Homologous and Heterologous Strains)

End point description:

The immunogenicity was assessed in terms of Geometric mean titer ratios (GMRs) of study day 29/study day 1, study day 50/study day 1, study day 181/study day 1 were evaluated.
The criteria for evaluation is GMR >2.5

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	165	83	
Units: Ratios				
geometric mean (confidence interval 95%)				
Day 29:1 A/Brisbane/2007 (A/H1N1) (N=165,163,82)	17 (15 to 20)	1.83 (1.57 to 2.13)	1.03 (0.83 to 1.27)	
Day 50:1 A/Brisbane/2007 (A/H1N1) (N=160,162,78)	83 (70 to 98)	4.55 (3.84 to 5.39)	1.11 (0.87 to 1.4)	
Day 181:1 A/Brisbane/2007 (A/H1N1) (N=161,163,80)	19 (17 to 21)	2.4 (2.11 to 2.73)	1.02 (0.85 to 1.22)	
Day 29:1 A/Brisbane/2007 (A/H3N2) (N=165,163,82)	15 (13 to 18)	1.58 (1.38 to 1.81)	1.07 (0.88 to 1.29)	
Day 50:1 A/Brisbane/2007 (A/H3N2) (N=160,162,78)	86 (73 to 102)	5.57 (4.73 to 6.55)	1.04 (0.83 to 1.32)	
Day 181:1 A/Brisbane/2007 (A/H3N2) (N=161,163,80)	30 (24 to 37)	6.16 (4.97 to 7.63)	2.1 (1.55 to 2.83)	
Day 29:1 B/Florida/2006 (N=165,163,82)	2.11 (1.86 to 2.39)	1.41 (1.24 to 1.6)	1.06 (0.89 to 1.26)	
Day 50:1 B/Florida/2006 (N=160,162,78)	14 (13 to 16)	2.05 (1.81 to 2.31)	1.02 (0.86 to 1.22)	
Day 181:1 B/Florida/2006 (N=161,163,80)	4.22 (3.79 to 4.68)	1.45 (1.31 to 1.61)	1.05 (0.91 to 1.22)	
Day 29:1A/SolomonIsland/2006(A/H1N1)(N	2.1 (1.81 to 2.42)	1.41 (1.22 to 1.62)	0.97 (0.79 to 1.18)	
Day 50:1A/SolomonIsland/2006(A/H1N1)(N	18 (16 to 21)	1.96 (1.7 to 2.25)	0.98 (0.8 to 1.19)	
Day181:1A/SolomonIsland/2006(A/H1N1)(N=161,163,80)	6.52 (5.79 to 7.34)	1.6 (1.42 to 1.8)	0.99 (0.84 to 1.16)	
Day 29:1 A/Wisconsin/2009 (A/H3N2)(N=165,163,82)	4.56 (4.07 to 5.11)	1.17 (1.05 to 1.31)	0.95 (0.81 to 1.11)	
Day 50:1 A/Wisconsin/2009 (A/H3N2)(N=160,162,78)	43 (37 to 50)	3.01 (2.59 to 3.51)	1.04 (0.84 to 1.29)	
Day181:1 A/Wisconsin/2009 (A/H3N2)(N=161,163,80)	20 (16 to 25)	5.06 (4.03 to 6.37)	2.22 (1.61 to 3.06)	
Day 29:1 B/Brisbane/2008 (N=164,163,82)	1.08 (1.04 to 1.11)	1.02 (0.098 to 1.05)	1 (0.96 to 1.05)	

Day 50:1 B/Brisbane/2008 (N=159,162,78)	1.94 (1.8 to 2.08)	1.11 (1.03 to 1.19)	1.02 (0.93 to 1.14)	
Day181:1 B/Brisbane/2008 (N=160,163,80)	1.04 (0.98 to 1.11)	1.05 (0.98 to 1.11)	1.26 (1.15 to 1.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: 12. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of Geometric Mean Titers (GMTs), in Unprimed Subjects Aged 6 to <36 Months for Season 2008/09 (Homologous and Heterologous Strains)

End point title	12. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of Geometric Mean Titers (GMTs), in Unprimed Subjects Aged 6 to <36 Months for Season 2008/09 (Homologous and Heterologous Strains)

End point description:

Immunogenicity was analyzed in terms of Geometric Mean Titers (GMTs) as measured by hemagglutination inhibition (HI) assay. For each strain and each vaccine group, least squares GMTs, associated 2-sided 95% confidence interval were determined for all time points.
Superiority analysis: GMT-TIV-adj/GMT-Flu-control >1 should be elicited to show that GMT-TIV-adj is superior to GMT-Flu-control

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	165	83	
Units: Titers				
geometric mean (confidence interval 95%)				
Day 1 A/Brisbane/2007 (A/H1N1)	6.21 (5.33 to 7.24)	7.52 (6.45 to 8.76)	5.93 (4.8 to 7.33)	
Day 29 A/Brisbane/2007 (A/H1N1) (N=165,163,82)	105 (82 to 136)	14 (11 to 18)	6.13 (4.33 to 8.69)	
Day 50 A/Brisbane/2007 (A/H1N1) (N=160,162,78)	513 (405 to 652)	35 (27 to 44)	6.57 (4.71 to 9.16)	
Day 181 A/Brisbane/2007 (A/H1N1) (N=161,163,80)	118 (95 to 146)	18 (15 to 22)	6.1 (4.51 to 8.25)	
Day 1 A/Brisbane/2007 (A/H3N2)	5.85 (5.13 to 6.67)	5.8 (5.09 to 6.6)	5.66 (4.73 to 6.77)	
Day 29 A/Brisbane/2007 (A/H3N2) (N=165,163,82)	90 (76 to 107)	9.17 (7.71 to 11)	6.04 (4.75 to 7.69)	
Day 50 A/Brisbane/2007 (A/H3N2) (N=160,162,78)	510 (426 to 609)	32 (27 to 39)	6 (4.68 to 7.68)	
Day 181 A/Brisbane/2007 (A/H3N2) (N=161,163,80)	176 (141 to 220)	36 (29 to 45)	12 (8.74 to 16)	
Day 1 B/Florida/2006	6.01 (5.59 to 6.45)	6 (5.59 to 6.44)	5.87 (5.32 to 6.47)	
Day 29 B/Florida/2006 (N=165,163,82)	13 (11 to 15)	8.45 (7.11 to 10)	6.19 (4.87 to 7.87)	

Day 50 B/Florida/2006 (N=160,162,78)	86 (74 to 100)	12 (11 to 14)	6.09 (4.95 to 7.49)	
Day 181 B/Florida/2006 (N=161,163,80)	25 (22 to 29)	8.72 (7.65 to 9.95)	6.21 (5.16 to 7.48)	
Day 1 A/SolomonIslands/2006(A/H1N1)	6.66 (5.56 to 7.98)	8.19 (6.85 to 9.8)	6.24 (4.87 to 8)	
Day 29 A/SolomonIslands/2006(A/H1N1)(N=16	14 (11 to 19)	12 (8.69 to 15)	6.08 (4.12 to 8.98)	
Day 50 A/SolomonIslands/2006(A/H1N1)(N=16	122 (94 to 157)	16 (13 to 21)	6.1 (4.27 to 8.73)	
Day181 A/SolomonIslands/2006(A/H1N1)(N=16	44 (34 to 55)	13 (10 to 17)	6.2 (4.46 to 8.61)	
Day 1 A/Wisconsin/2009 (A/H3N2)	6.09 (5.26 to 7.06)	6.74 (5.83 to 7.8)	6.16 (5.03 to 7.53)	
Day 29 A/Wisconsin/2009 (A/H3N2)(N=165,163,82)	28 (23 to 33)	7.86 (6.57 to 9.39)	5.87 (4.59 to 7.52)	
Day 50 A/Wisconsin/2009 (A/H3N2)(N=160,162,78)	261 (218 to 313)	20 (17 to 24)	6.47 (5.03 to 8.32)	
Day181 A/Wisconsin/2009(A/H3N2)(N=161,163,	123 (97 to 156)	34 (27 to 43)	14 (9.81 to 19)	
Day 1 B/Brisbane/2008 (N=165,165,83)	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)	
Day 29 B/Brisbane/2008 (N=165,163,82)	5.38 (5.21 to 5.56)	5.08 (4.91 to 5.24)	5 (4.78 to 5.23)	
Day 50 B/Brisbane/2008 (N=160,162,78)	9.64 (8.96 to 10)	5.55 (5.16 to 5.97)	5.12 (4.63 to 5.68)	
Day181 B/Brisbane/2008 (N=161,163,80)	5.21 (4.89 to 5.54)	5.23 (4.92 to 5.56)	6.28 (5.75 to 6.84)	

Statistical analyses

Statistical analysis title	GMT A/H1N1; Day 1-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay.

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.02

Statistical analysis title	GMT A/H1N1; Day 29-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay.

Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	7.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.42
upper limit	11

Statistical analysis title	GMT A/H1N1; Day 50-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	15
Confidence interval	
level	95 %
sides	2-sided
lower limit	11
upper limit	21

Statistical analysis title	GMT A/H1N1; Day 181-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	6.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.83
upper limit	8.68

Statistical analysis title	GMT A/H3N2; Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.21

Statistical analysis title	GMT A/H3N2; Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	9.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.76
upper limit	12

Statistical analysis title	GMT A/H3N2; Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	20

Statistical analysis title	GMT A/H3N2; Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	4.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.64
upper limit	6.65

Statistical analysis title	GMT B; Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[B/Florida/2006]
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.1

Statistical analysis title	GMT B; Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Florida/2006]
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	1.9

Statistical analysis title	GMT B; Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Florida/2006]
Point estimate	6.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.72
upper limit	8.53

Statistical analysis title	GMT B; Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Florida/2006]
Point estimate	2.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.44
upper limit	3.5

Statistical analysis title	GMT A/H1N1 (Hetero); Day 1-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay.

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.04

Statistical analysis title	GMT A/H1N1 (Hetero); Day 29-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay.

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.78

Statistical analysis title	GMT A/H1N1 (Hetero); Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	7.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.33
upper limit	11

Statistical analysis title	GMT A/H1N1(Hetero); Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <36 months by HI assay	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	3.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	4.55

Statistical analysis title	GMT A/H3N2 (Hetero); Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.1

Statistical analysis title	GMT A/H3N2 (Hetero); Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	3.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.78
upper limit	4.51

Statistical analysis title	GMT A/H3N2 (Hetero); Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	10
upper limit	16

Statistical analysis title	GMT A/H3N2(Hetero); Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	Flu-control v TIV-adj
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.61
upper limit	4.95

Statistical analysis title	GMT B (Hetero); Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1

Statistical analysis title	GMT B (Hetero); Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.11

Statistical analysis title	GMT B (Hetero); Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	1.92

Statistical analysis title	GMT B (Hetero); Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <36 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.08

Secondary: 13. Percentage (95% CI) of Unprimed Subjects Aged 6 to <36 Months With HI Titer ≥1:40 in Season 2008/09 HI Assay (Homologous and Heterologous Strains)

End point title	13. Percentage (95% CI) of Unprimed Subjects Aged 6 to <36 Months With HI Titer ≥1:40 in Season 2008/09 HI Assay (Homologous and Heterologous Strains)

End point description:

Percentage of subjects achieving seroprotection (i.e., with HI titer ≥1:40) at study day 1, study day 29, study day 50 and a study day 181 and associated 95% CI. The lower bound of the two-sided 95% CI for the percentage of subjects achieving an HI antibody titer ≥1:40 should meet or exceed 70%.

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj (6 to <36 Months)-Safety	Flu-control (6 to <36 Months)-Safety	Non-flu control (TBE/Men C Vaccine)-Safety	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	166	165	83	
Units: Percentages of subjects				
number (confidence interval 95%)				
Day 1 A/Brisbane/2007 (A/H1N1)	5 (3 to 10)	11 (7 to 17)	5 (1 to 12)	
Day 29 A/Brisbane/2007 (A/H1N1) (N=165,163,82)	92 (86 to 95)	20 (14 to 27)	6 (2 to 14)	
Day 50 A/Brisbane/2007 (A/H1N1) (N=160,162,78)	100 (98 to 100)	38 (31 to 46)	6 (2 to 14)	
Day 181 A/Brisbane/2007 (A/H1N1) (N=161,163,80)	98 (94 to 99)	25 (19 to 33)	6 (2 to 14)	
Day 1 A/Brisbane/2007 (A/H3N2)	4 (1 to 8)	4 (1 to 8)	2 (0 to 8)	
Day 29 A/Brisbane/2007 (A/H3N2) (N=165,163,82)	95 (90 to 97)	12 (7 to 18)	4 (1 to 10)	
Day 50 A/Brisbane/2007 (A/H3N2) (N=160,162,78)	99 (97 to 100)	45 (37 to 53)	4 (1 to 11)	
Day 181 A/Brisbane/2007 (A/H3N2) (N=161,163,80)	100 (98 to 100)	45 (37 to 53)	21 (13 to 32)	
Day 1 B/Florida/2006	2 (1 to 6)	2 (0 to 5)	1 (0.03 to 7)	
Day 29 B/Florida/2006 (N=165,163,82)	12 (8 to 18)	12 (8 to 18)	4 (1 to 10)	
Day 50 B/Florida/2006 (N=160,162,78)	88 (81 to 92)	19 (13 to 25)	3 (0 to 9)	
Day 181 B/Florida/2006 (N=161,163,80)	40 (33 to 48)	13 (9 to 20)	3 (0 to 9)	
Day 1 A/SolomonIslands/2006(A/H1N1)	5 (3 to 10)	11 (7 to 17)	5 (1 to 12)	
Day 29 A/SolomonIslands/2006(A/H1N1)(N=16	15 (10 to 21)	13 (9 to 20)	5 (1 to 12)	
Day 50 A/SolomonIslands/2006(A/H1N1)(N=16	95 (90 to 98)	24 (18 to 31)	5 (1 to 13)	
Day181 A/SolomonIslands/2006(A/H1N1)(N=16	61 (53 to 68)	19 (13 to 26)	5 (1 to 12)	
Day 1 A/Wisconsin/2009 (A/H3N2)	4 (1 to 8)	5 (2 to 9)	2 (0 to 8)	
Day 29 A/Wisconsin/2009 (A/H3N2)(N=165,163,82)	37 (30 to 45)	6 (3 to 10)	2 (0 to 9)	

Day 50 A/Wisconsin/2009 (A/H3N2)(N=160,162,78)	100 (98 to 100)	30 (23 to 37)	4 (1 to 11)	
Day181 A/Wisconsin/2009 (A/H3N2)(N=161,163,80)	99 (97 to 100)	42 (34 to 50)	23 (14 to 33)	
Day 1 B/Brisbane/2008 (N=166,165,83)	0 (0 to 2)	0 (0 to 2)	0 (0 to 4)	
Day 29 B/Brisbane/2008 (N=165,163,82)	1 (0.015 to 3)	0 (0 to 2)	0 (0 to 4)	
Day 50 B/Brisbane/2008 (N=160,162,78	5 (2 to 10)	0 (0 to 2)	0 (0 to 5)	
Day181 B/Brisbane/2008 (N=161,163,80)	0 (0 to 2)	1 (0.016 to 3)	6 (2 to 14)	

Statistical analyses

No statistical analyses for this end point

Secondary: 14. Percentage (95% CI) of Unprimed Subjects Aged 6 to <36 Months With Seroconversion From Baseline, for Season 2008/09 (Homologous and Heterologous Strains)

End point title	14. Percentage (95% CI) of Unprimed Subjects Aged 6 to <36 Months With Seroconversion From Baseline, for Season 2008/09 (Homologous and Heterologous Strains)

End point description:

HI assay was used for the analysis. Seroconversion is defined as negative pre-vaccination serum (<10)/ post-vaccination HI titer ≥1:40.
Seroconversion is defined as either pre-vaccination HI titer <10 and a post-vaccination HI titer ≥1:40 or a prevaccination HI titer ≥10 and a minimum four-fold rise in post-vaccination HI antibody titer.
The lower bound of the two-sided 95% confidence interval (CI) for the percentage of subjects achieving seroconversion for HI antibody should meet or exceed 40%.

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	165	163	82	
Units: Percentages of subjects				
number (confidence interval 95%)				
Day29 A/Brisbane/2007(A/H1N1)	92 (86 to 95)	19 (13 to 26)	1 (0.031 to 7)	
Day50 A/Brisbane/2007(A/H1N1)(N=160,162,7	100 (98 to 100)	38 (30 to 46)	1 (0.032 to 7)	
Day181A/Brisbane/2007(A/H1N1)(N=16 1,163,80)	97 (93 to 99)	24 (18 to 31)	1 (0.032 to 7)	
Day29 A/Brisbane/2007(A/H3N2)	93 (88 to 97)	10 (6 to 16)	1 (0.031 to 7)	
Day50 A/Brisbane/2007(A/H3N2)(N=160,162,7	98 (95 to 100)	44 (36 to 52)	1 (0.032 to 7)	
Day181A/Brisbane/2007(A/H3N2)(N=16 1,163,80)	98 (94 to 99)	42 (35 to 50)	19 (11 to 29)	
Day29 B/Florida/2006	12 (8 to 18)	12 (8 to 18)	0 (0 to 4)	
Day50 B/Florida/2006 (N=160,162,78)	88 (81 to 92)	19 (13 to 25)	0 (0 to 5)	
Day181B/Florida/2006 (N=161,163,80)	39 (31 to 46)	12 (7 to 18)	1 (0.032 to 7)	

Day29A/Sol.Islands/2006(A/H1N1)	14 (9 to 20)	13 (8 to 19)	0 (0 to 4)	
Day50A/Sol.Islands/2006(A/H1N1)(N=160,162,78)	94 (89 to 97)	23 (17 to 30)	0 (0 to 5)	
Day181A/Sol.Islands/2006(A/H1N1)(N=161,163,80)	60 (52 to 68)	18 (12 to 25)	0 (0 to 5)	
Day29 A/Wisconsin/2009(A/H3N2)	36 (28 to 44)	4 (1 to 8)	0 (0 to 4)	
Day50 A/Wisconsin/2009(A/H3N2)(N=160,162,	100 (98 to 100)	27 (20 to 35)	1 (0.032 to 7)	
Day181A/Wisconsin/2009(A/H3N2)(N=161,163,80)	97 (93 to 99)	39 (31 to 47)	20 (12 to 30)	
Day29 B/Brisbane/2008	1 (0.015 to 3)	0 (0 to 2)	0 (0 to 45)	
Day 50:1 B/Brisbane/2008 (N=160,162,78)	5 (2 to 12)	0 (0 to 2)	0 (0 to 5)	
Day181 B/Brisbane/2008 (N=161,163,80)	0 (0 to 2)	1 (0.016 to 3)	6 (2 to 14)	

Statistical analyses

No statistical analyses for this end point

Secondary: 15. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of Geometric Mean Titers (GMTs), in Unprimed Subjects Aged 6 to <72 Months for Season 2008/09 (Homologous and Heterologous Strains)

End point title	15. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of Geometric Mean Titers (GMTs), in Unprimed Subjects Aged 6 to <72 Months for Season 2008/09 (Homologous and Heterologous Strains)

End point description:

Immunogenicity was analyzed in terms of Geometric Mean Titers (GMTs) as measured by hemagglutination inhibition (HI) assay. For each strain and each vaccine group, least squares GMTs, associated 2-sided 95% confidence interval were determined for all time points Superiority analysis: GMT-TIV-adj/GMT-Flu-control >1 and GMT-TIV-adj/GMT-Non Flu control >1 should be elicited to show that GMT-TIV-adj is superior to GMT-Flu-control/Non Flu-control

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	319	316	158	
Units: Titers				
geometric mean (confidence interval 95%)				
Day 1 A/Brisbane/2007 (A/H1N1)	9.63 (8.28 to 11)	10 (8.59 to 12)	9.48 (7.67 to 12)	
Day29A/Brisbane/2007(A/H1N1) (N=316,313,156)	232 (185 to 291)	36 (29 to 45)	9.42 (6.85 to 13)	
Day50A/Brisbane/2007(A/H1N1) (N=310,309,150)	735 (608 to 888)	89 (74 to 108)	9.91 (7.58 to 13)	
Day181A/Brisbane/2007(A/H1N1) (N=309,310,151)	186 (155 to 225)	43 (35 to 51)	9.65 (7.41 to 13)	
Day1A/Brisbane/2007(A/H3N2)	12 (10 to 15)	12 (9.83 to 14)	12 (8.98 to 15)	

Day 29 A/Brisbane/2007 (A/H3N2) (N=316,313,156)	209 (167 to 261)	33 (26 to 41)	12 (8.83 to 17)	
Day 50 A/Brisbane/2007 (A/H3N2) (N=310,309,150)	762 (634 to 915)	95 (79 to 115)	12 (9.18 to 15)	
Day 181 A/Brisbane/2007 (A/H3N2) (N=309,310,151)	295 (245 to 356)	94 (78 to 114)	26 (20 to 34)	
Day 1 B/Florida/2006	6.37 (6.01 to 6.75)	6.57 (6.2 to 6.96)	6.41 (5.92 to 6.95)	
Day 29 B/Florida/2006 (N=316,313,156)	21 (18 to 25)	14 (12 to 16)	6.54 (5.26 to 8.13)	
Day 50 B/Florida/2006 (N=310,309,150)	109 (97 to 123)	22 (19 to 25)	6.67 (5.64 to 7.88)	
Day 181 B/Florida/2006 (N=309,310,151)	32 (29 to 36)	13 (11 to 14)	6.92 (6.01 to 7.98)	
Day 1 A/SolomonIslands/2006(A/H1N1)	11 (9.47 to 14)	12 (9.89 to 14)	10 (8.16 to 13)	
Day29 A/SolomonIslands/2006(A/H1N1)(N=31	40 (30 to 53)	23 (18 to 31)	10 (7.12 to 15)	
Day50 A/SolomonIslands/2006(A/H1N1)(N=31	228 (182 to 287)	41 (33 to 51)	11 (7.63 to 15)	
Day181A/SolomonIslands/2006(A/H1N1)(N=309,310,151)	88 (70 to 109)	28 (23 to 35)	11 (7.76 to 14)	
Day 1 A/Wisconsin/2009 (A/H3N2)	15 (12 to 18)	15 (12 to 19)	13 (9.97 to 18)	
Day 29 A/Wisconsin/2009 (A/H3N2) (N=316,313,156)	98 (75 to 127)	31 (24 to 40)	13 (8.74 to 18)	
Day 50 A/Wisconsin/2009 (A/H3N2) (N=310,309,150)	518 (420 to 639)	70 (57 to 87)	14 (10 to 19)	
Day181 A/Wisconsin/2009 (A/H3N2) (N=309,310,151)	261 (212 to 322)	98 (79 to 121)	34 (26 to 46)	
Day 1 B/Brisbane/2008)	5.05 (4.99 to 5.11)	5.05 (5 to 5.11)	5.08 (5 to 5.16)	
Day 29 B/Brisbane/2008 (N=316,313,156)	6.31 (5.97 to 6.66)	5.57 (5.28 to 5.89)	5.11 (4.74 to 5.52)	
Day 50 B/Brisbane/2008 (N=310,309,150)	12 (11 to 13)	6.69 (6.23 to 7.17)	5.2 (4.71 to 5.75)	
Day181 B/Brisbane/2008 (N=309,310,151)	6.12 (5.77 to 6.49)	5.67 (5.35 to 6.01)	6.12 (5.64 to 6.65)	

Statistical analyses

Statistical analysis title	GMT A/H1N1; Day 1-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay.

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.19

Statistical analysis title	GMT A/H1N1; Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	6.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.69
upper limit	8.76

Statistical analysis title	GMT A/H1N1; Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay	
Comparison groups	Flu-control v TIV-adj
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	8.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.36
upper limit	11

Statistical analysis title	GMT A/H1N1; Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Brisbane/2007 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H1N1)]
Point estimate	4.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.38
upper limit	5.65

Statistical analysis title	GMT A/H3N2; Day 1-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.35

Statistical analysis title	GMT A/H3N2; Day 29-TIV-adj vs Flu-control

Statistical analysis description:

To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.

Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	6.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.72
upper limit	8.73

Statistical analysis title	GMT A/H3N2; Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	7.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.2
upper limit	10

Statistical analysis title	GMT A/H3N2; Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Brisbane/2007 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[A/Brisbane/2007 (A/H3N2)]
Point estimate	3.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.42
upper limit	4.05

Statistical analysis title	GMT B; Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[B/Florida/2006]
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.05

Statistical analysis title	GMT B; Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[B/Florida/2006]
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	1.93

Statistical analysis title	GMT B; Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[B/Florida/2006]
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.25
upper limit	5.88

Statistical analysis title	GMT B; Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain B/Florida/2006 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT[B/Florida/2006]
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.22
upper limit	2.93

Statistical analysis title	GMT A/H1N1 (Hetero); Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.22

Statistical analysis title	GMT A/H1N1 (Hetero); Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	2.51

Statistical analysis title	GMT A/H1N1 (Hetero); Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	5.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.08
upper limit	7.63

Statistical analysis title	GMT A/H1N1(Hetero); Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Solomon Islands/2006 (A/H1N1) in terms of GMTs in subjects aged 6 to <72 months by HI assay	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Solomon Islands/2006 (A/H1N1)]
Point estimate	3.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	4.2

Statistical analysis title	GMT A/H3N2 (Hetero); Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.3

Statistical analysis title	GMT A/H3N2 (Hetero); Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	3.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.19
upper limit	4.49

Statistical analysis title	GMT A/H3N2 (Hetero); Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	7.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.51
upper limit	9.82

Statistical analysis title	GMT A/H3N2(Hetero); Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain A/Wisconsin/2009 (A/H3N2) in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [A/Wisconsin/2009 (A/H3N2)]
Point estimate	2.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	3.55

Statistical analysis title	GMT B (Hetero); Day 1-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 1 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.01

Statistical analysis title	GMT B (Hetero); Day 29-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 29 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.22

Statistical analysis title	GMT B (Hetero); Day 50-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 50 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control
Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	1.97

Statistical analysis title	GMT B (Hetero); Day 181-TIV-adj vs Flu-control
Statistical analysis description:	
To demonstrate superiority of immunogenicity of TIV-adj compared to Flu-control on Day 181 for strain B/Brisbane/2008 in terms of GMTs in subjects aged 6 to <72 months by HI assay.	
Comparison groups	TIV-adj v Flu-control

Number of subjects included in analysis	635
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANOVA
Parameter estimate	GMT [B/Brisbane/2008]
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.17

Secondary: 16. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of GMRs, in Unprimed Subjects Aged 6 to <72 Months for Season 2008/09 (Homologous and Heterologous Strains)

End point title	16. Immunogenicity of aTIV, Compared to Flu and Non-Flu-control, in Terms of GMRs, in Unprimed Subjects Aged 6 to <72 Months for Season 2008/09 (Homologous and Heterologous Strains)

End point description:

Hemagglutination Inhibition (HI) assay was used for the analysis. Geometric mean titer ratios (GMRs) of study day 29/study day 1, study day 50/study day 1, study day 181/study day 1 were evaluated. The criteria for evaluation is GMR >2.5

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	319	316	158	
Units: Ratio				
geometric mean (confidence interval 95%)				
Day 29:1A/Brisbane/2007(A/H1N1;N=316,3	24 (21 to 27)	3.6 (3.17 to 4.08)	0.99 (0.83 to 1.18)	
Day 50:1A/Brisbane/2007(A/H1N1;N=310,3	76 (67 to 86)	9 (7.89 to 10)	1.02 (0.84 to 1.22)	
Day 181:1A/Brisbane/2007(A/H1N1;N=309,	19 (17 to 21)	4.31 (3.89 to 4.77)	1.02 (0.88 to 1.17)	
Day 29:1A/Brisbane/2007(A/H3N2;N=316,3	17 (15 to 19)	2.73 (2.4 to 3.09)	1.03 (0.86 to 1.23)	
Day50:1A/Brisbane/2007(A/H3N2;N=310,309,150)	60 (52 to 69)	8.03 (6.93 to 9.3)	0.98 (0.8 to 1.21)	
Day 181:1A/Brisbane/2007(A/H3N2;N=309,	24 (20 to 28)	7.96 (6.71 to 9.44)	2.21 (1.73 to 2.81)	
Day 29:1B/Florida/2006(N=316,313,156)	3.32 (2.94 to 3.75)	2.06 (1.83 to 2.33)	1.03 (0.87 to 1.22)	
Day 50:1B/Florida/2006(N=310,309,150)	17 (15 to 19)	3.29 (2.98 to 3.63)	1.03 (0.9 to 1.18)	

Day 181:1B/Florida/2006(N=309,310,151)	5.05 (4.67 to 5.46)	1.92 (1.78 to 2.08)	1.06 (0.95 to 1.19)	
Day 29:1A/Sol.Island/2006(A/H1N1;N=316,	3.51 (3.09 to 3.98)	1.96 (1.72 to 2.22)	0.99 (0.83 to 1.14)	
Day 50:1A/Sol.Island/2006A/H1N1;N=310,3	20 (18 to 22)	3.49 (3.12 to 3.89)	0.97 (0.83 to 1.14)	
Day 181:1A/Sol.Island/2006A/H1N1;N=309,	7.63 (6.98 to 8.34)	2.41 (2.2 to 2.63)	1.01 (0.89 to 1.14)	
Day 29:1A/Wisconsin/2009(A/H3N2;N=316,	6.59 (5.92 to 7.34)	2.04 (1.83 to 2.27)	0.93 (0.8 to 1.09)	
Day 50:1A/Wisconsin/2009(A/H3N2;N=310,	34 (30 to 38)	4.6 (4.07 to 5.2)	0.98 (0.83 to 1.17)	
Day 181:1A/Wisconsin/2009(A/H3N2;N=309	18 (15 to 21)	6.69 (5.36 to 7.6)	2.59 (2 to 3.29)	
Day 29:1B/Brisbane/2008(N=315,313,156)	1.25 (1.19 to 1.31)	1.1 (1.05 to 1.16)	1.01 (0.94 to 1.08)	
Day 50:1B/Brisbane/2008(N=309,309,150)	2.38 (2.23 to 2.55)	1.32 (1.24 to 1.42)	1.02 (0.93 to 1.13)	
Day 181:1B/Brisbane/2008(N=308,310,151)	1.21 (1.15 to 1.28)	1.12 (1.06 to 1.19)	1.21 (1.11 to 1.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: 17. Percentages of Subjects With HI Titers ≥ 1:40 in Unprimed Subjects 6 to <72 Months of Age for Season 2008/09 Homologous and Heterologous Strains

End point title	17. Percentages of Subjects With HI Titers ≥ 1:40 in Unprimed Subjects 6 to <72 Months of Age for Season 2008/09 Homologous and Heterologous Strains

End point description:

Hemagglutination Inhibition (HI) assay was used for the analysis.
Percentage of subjects achieving seroprotection (i.e., with HI titer ≥1:40) at study day 1, study day 29, study day 50 and a study day 181 and associated 95% Confidence Intervals. The lower bound of the two-sided 95% CI for the percentage of subjects achieving an HI antibody titer ≥1:40 should meet or exceed 70%.

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	319	316	158	
Units: Percentages of subjects				
number (confidence interval 95%)				
Day 1 A/Brisbane/2007 (A/H1N1)	20 (16 to 25)	21 (17 to 26)	16 (11 to 23)	
Day29A/Brisbane/2007(A/H1N1) (N=316,313,156)	96 (93 to 98)	40 (35 to 46)	17 (11 to 23)	
Day50A/Brisbane/2007(A/H1N1) (N=310,309,150)	100 (99 to 100)	59 (54 to 65)	17 (12 to 24)	

Day181A/Brisbane/2007(A/H1N1) (N=309,310,151)	98 (96 to 99)	49 (43 to 54)	18 (12 to 25)	
Day1A/Brisbane/2007(A/H3N2)	23 (18 to 28)	22 (17 to 27)	20 (14 to 27)	
Day 29 A/Brisbane/2007 (A/H3N2) (N=316,313,156)	96 (93 to 98)	35 (30 to 40)	21 (15 to 28)	
Day 50 A/Brisbane/2007 (A/H3N2) (N=310,309,150)	99 (97 to 100)	65 (60 to 71)	21 (14 to 28)	
Day 181 A/Brisbane/2007 (A/H3N2) (N=309,310,151)	100 (98 to 100)	65 (60 to 70)	41 (33 to 49)	
Day 1 B/Florida/2006	2 (1 to 4)	2 (1 to 5)	4 (1 to 8)	
Day 29 B/Florida/2006 (N=316,313,156)	28 (23 to 33)	26 (21 to 31)	4 (1 to 8)	
Day 50 B/Florida/2006 (N=310,309,150)	93 (89 to 95)	38 (33 to 44)	3 (1 to 8)	
Day 181 B/Florida/2006 (N=309,310,151)	52 (46 to 57)	23 (18 to 28)	4 (1 to 8)	
Day 1 A/SolomonIslands/2006(A/H1N1)	21 (16 to 26)	22 (17 to 27)	18 (12 to 25)	
Day29 A/SolomonIslands/2006(A/H1N1)(N=31	32 (27 to 38)	24 (20 to 29)	18 (12 to 25)	
Day50 A/SolomonIslands/2006(A/H1N1)(N=31	96 (94 to 98)	45 (39 to 51)	18 (12 to 25)	
Day181A/SolomonIslands/2006(A/H1N1)(N=309,310,151)	72 (67 to 77)	34 (29 to 40)	18 (12 to 25)	
Day 1 A/Wisconsin/2009 (A/H3N2)	25 (21 to 31)	25 (20 to 30)	21 (15 to 28)	
Day 29 A/Wisconsin/2009 (A/H3N2) (N=316,313,156)	60 (54 to 66)	29 (24 to 34)	21 (14 to 28)	
Day 50 A/Wisconsin/2009 (A/H3N2) (N=310,309,150)	100 (98 to 100)	54 (48 to 59)	21 (15 to 29)	
Day181 A/Wisconsin/2009 (A/H3N2) (N=309,310,151)	100 (98 to 100)	63 (57 to 68)	43 (35 to 51)	
Day 1 B/Brisbane/2008)	0 (0 to 1)	0 (0 to 1)	1 (0.016 to 3)	
Day 29 B/Brisbane/2008 (N=316,313,156)	3 (2 to 6)	1 (0 to 3)	1 (0.016 to 4)	
Day 50 B/Brisbane/2008 (N=310,309,150)	10 (7 to 14)	3 (1 to 5)	0 (0 to 2)	
Day181 B/Brisbane/2008 (N=309,310,151)	3 (1 to 5)	3 (1 to 5)	5 (2 to 10)	

Statistical analyses

No statistical analyses for this end point

Secondary: 18. Percentages of Subjects With Seroconversion and Vaccine Group Differences in Unprimed Subjects 6 to <72 Months of Age for Season 2008/09 (Homologous and Heterologous Strains)

End point title	18. Percentages of Subjects With Seroconversion and Vaccine Group Differences in Unprimed Subjects 6 to <72 Months of Age for Season 2008/09 (Homologous and Heterologous Strains)

End point description:

HI assay was used for the analysis. Seroconversion is defined as negative pre-vaccination serum (<10)/ post-vaccination HI titer ≥1:40.
Seroconversion is defined as either pre-vaccination HI titer <10 and a post-vaccination HI titer ≥1:40 or a prevaccination HI titer ≥10 and a minimum 4-fold rise in post-vaccination HI antibody titer. The lower bound of the two-sided 95% confidence interval (CI) for the percentage of subjects achieving seroconversion for HI antibody should meet or exceed 40%.

End point type	Secondary

End point timeframe:

On study days 1, 29, 50 and 181

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	319	316	158	
Units: Ratios				
geometric mean (confidence interval 95%)				
Day 29:1A/Brisbane/2007(A/H1N1;N=316,3	96 (93 to 98)	40 (34 to 45)	1 (0.016 to 4)	
Day 50:1A/Brisbane/2007(A/H1N1;N=10,30	100 (99 to 100)	59 (53 to 64)	1 (0 to 5)	
Day 181:1A/Brisbane/2007(A/H1N1;N=309,	98 (96 to 99)	48 (42 to 53)	1 (0 to 5)	
Day 29:1A/Brisbane/2007(A/H3N2;N=316,3	94 (91 to 97)	31 (26 to 37)	1 (0.016 to 4)	
Day 50:1A/Brisbane/2007(A/H3N2;N=310,3	97 (95 to 99)	63 (57 to 68)	2 (0 to 6)	
Day 181:1A/Brisbane/2007(A/H3N2;N=309,	93 (90 to 96)	56 (51 to 62)	23 (17 to 31)	
Day 29:1B/Florida/2006(N=316,313,156)	28 (23 to 33)	26 (21 to 31)	0 (0 to 2)	
Day 50:1B/Florida/2006(N=310,309,150)	93 (89 to 95)	38 (32 to 43)	1 (0.017 to 4)	
Day 181:1B/Florida/2006(N=309,310,151)	50 (44 to 56)	19 (15 to 24)	1 (0 to 5)	
Day 29:1A/Sol.Island/2006(A/H1N1;N=316,	32 (27 to 37)	24 (19 to 29)	0 (0 to 2)	
Day 50:1A/Sol.Island/2006A/H1N1;N=310,3	96 (93 to 98)	44 (39 to 50)	0 (0 to 2)	
Day 181:1A/Sol.Island/2006A/H1N1;N=309,	72 (66 to 76)	33 (27 to 38)	0 (0 to 2)	
Day 29:1A/Wisconsin/2009(A/H3N2;N=316,	58 (53 to 64)	23 (19 to 28)	1 (0.016 to 4)	
Day 50:1A/Wisconsin/2009(A/H3N2;N=310,	98 (96 to 99)	49 (43 to 54)	2 (0 to 6)	
Day 181:1A/Wisconsin/2009(A/H3N2;N=309	92 (89 to 95)	52 (46 to 58)	25 (18 to 33)	
Day 29:1B/Brisbane/2008(N=315,313,156)	3 (2 to 6)	1 (0 to 3)	0 (0 to 2)	
Day 50:1B/Brisbane/2008(N=309,309,150)	10 (7 to 14)	3 (1 to 5)	0 (0 to 2)	
Day 181:1B/Brisbane/2008(N=308,310,151)	2 (1 to 5)	3 (1 to 5)	5 (2 to 10)	

Statistical analyses

No statistical analyses for this end point

Secondary: 19. Number of Subjects With Local and Systemic Reactions for Egg and

Cell Derived Inactivated Novel Swine Origin A/H1N1 Subunit Influenza Vaccines After Each Vaccination for All Seasons

End point title	19. Number of Subjects With Local and Systemic Reactions for Egg and Cell Derived Inactivated Novel Swine Origin A/H1N1 Subunit Influenza Vaccines After Each Vaccination for All Seasons

End point description:

Adequate data was not available to conduct this analysis.

End point type	Secondary

End point timeframe:

7 days post-vaccination

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: Subjects				

Notes:

[2] - Adequate data was not available to conduct this analysis.

[3] - Adequate data was not available to conduct this analysis.

[4] - Adequate data was not available to conduct this analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: 20. Indirect Protective Effect of Fluad (NH Composition 2007/2008), Compared to Non-flu and Flu Control, in Connection to Household-contact Persons Via Questioning of the Parents About ILI of Persons Living in the Same Household as the Study Child

End point title	20. Indirect Protective Effect of Fluad (NH Composition 2007/2008), Compared to Non-flu and Flu Control, in Connection to Household-contact Persons Via Questioning of the Parents About ILI of Persons Living in the Same Household as the Study Child

End point description:

As per an amendment to the protocol, the Secondary efficacy endpoints were evaluated in enrolled subjects only and the household members were not included in the trial for the evaluation of indirect vaccine efficacy.

End point type	Secondary

End point timeframe:

3 weeks after 2nd vaccination

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: Subjects				

Notes:

[5] - Adequate data was not available to conduct this analysis.

[6] - Adequate data was not available to conduct this analysis.

[7] - Adequate data was not available to conduct this analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: 21. Incidence Rate of the 2009-2010 H1N1 Swine Pandemic Caused by a Novel Influenza A (H1N1) Virus of Swine Origin in Unprimed Children Aged 6 to <36 and 6 to <72 Months

End point title	21. Incidence Rate of the 2009-2010 H1N1 Swine Pandemic Caused by a Novel Influenza A (H1N1) Virus of Swine Origin in Unprimed Children Aged 6 to <36 and 6 to <72 Months

End point description:

Adequate data was not available for assessing the incidence rates of the 2009-2010 swine pandemic caused by a novel influenza A (H1N1) virus of swine origin.

End point type	Secondary

End point timeframe:

3 weeks after 2nd vaccination

End point values	TIV-adj	Flu-control	Non-flu Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Incidence				

Notes:

[8] - Adequate data was not available to conduct this analysis.

[9] - Adequate data was not available to conduct this analysis.

[10] - Adequate data was not available to conduct this analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 3 years (3 consecutive influenza seasons: 2007/08, 2008/09 and 2009/10).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12

Reporting groups	
Reporting group title	TIV-adj_0.25
Reporting group description: Subjects aged 6 to < 36 months received 0.25 mL of each injection of adjuvanted trivalent inactivated subunit influenza vaccine	
Reporting group title	TIV-adj_0.5
Reporting group description: Subjects aged 36 to < 72 months received 0.5 mL of each injection of adjuvanted trivalent inactivated subunit influenza vaccine	
Reporting group title	Flu-control_0.25
Reporting group description: Subjects aged 6 to < 36 months received 0.25 mL of each injection of non-adjuvanted trivalent inactivated subunit influenza vaccine or non-adjuvanted trivalent inactivated split influenza vaccine	
Reporting group title	Flu-control_0.5
Reporting group description: Subjects aged 36 to < 72 months received 0.5 mL of each injection of non-adjuvanted trivalent inactivated subunit influenza vaccine or non-adjuvanted trivalent inactivated split influenza vaccine	
Reporting group title	Non-Flu-control (TBE/Men C Vaccine)
Reporting group description: Subjects aged 6 to <12 months received 2 doses of 0.5 mL of Novartis Menningocoocal C conjugate vaccine and subjects aged 12 to <72 months received 2 doses of 0.25 mL of Tick-borne encephalitis (TBE) vaccine	
Reporting group title	Non-Flu-control (TBE vaccine)
Reporting group description: subjects aged 12 to <72 months received 2 doses of 0.25 mL of TBE vaccine.	

Serious adverse events	TIV-adj_0.25	TIV-adj_0.5	Flu-control_0.25
Total subjects affected by serious adverse events			
subjects affected / exposed	91 / 1177 (7.73%)	31 / 835 (3.71%)	104 / 1069 (9.73%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	1 / 1177 (0.08%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain tumour operation			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patent ductus arteriosus repair			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toe amputation			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillectomy			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Developmental delay			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbances			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 1177 (0.17%)	1 / 835 (0.12%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Child abuse			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	2 / 1177 (0.17%)	0 / 835 (0.00%)	2 / 1069 (0.19%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis chronic			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			

subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar disorder			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar haemorrhage			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphemia			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abnormal behaviour			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Paracentesis			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonoscopy			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental exposure			
subjects affected / exposed	2 / 1177 (0.17%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	6 / 1177 (0.51%)	2 / 835 (0.24%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	2 / 1177 (0.17%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug toxicity			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electric shock			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Humerus fracture			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineal injury			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture base			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord injury			

subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic brain injury			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaccination failure			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod bite			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental poisoning			

subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Acquired epileptic aphasia			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	1 / 1177 (0.08%)	1 / 835 (0.12%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	2 / 1177 (0.17%)	1 / 835 (0.12%)	4 / 1069 (0.37%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Petit mal epilepsy			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphthous stomatitis			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			

subjects affected / exposed	2 / 1177 (0.17%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	3 / 1069 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malabsorption			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema multiforme			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Henoch-Schonlein purpura			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urticaria			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photosensitivity reaction			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			

subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod infestation			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	8 / 1177 (0.68%)	3 / 835 (0.36%)	7 / 1069 (0.65%)
occurrences causally related to treatment / all	0 / 12	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 1177 (0.00%)	1 / 835 (0.12%)	2 / 1069 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter infection			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum			

subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	14 / 1177 (1.19%)	1 / 835 (0.12%)	13 / 1069 (1.22%)
occurrences causally related to treatment / all	0 / 14	0 / 1	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 1177 (0.08%)	1 / 835 (0.12%)	5 / 1069 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	12 / 1177 (1.02%)	8 / 835 (0.96%)	39 / 1069 (3.65%)
occurrences causally related to treatment / all	0 / 12	0 / 8	0 / 39
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			

subjects affected / exposed	1 / 1177 (0.08%)	1 / 835 (0.12%)	2 / 1069 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	2 / 1177 (0.17%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal infection			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			

subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 1177 (0.42%)	2 / 835 (0.24%)	5 / 1069 (0.47%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudocroup			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	2 / 1069 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	4 / 1177 (0.34%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	2 / 1177 (0.17%)	1 / 835 (0.12%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	2 / 1177 (0.17%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsilitis			

subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	2 / 1069 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	2 / 1069 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotavirus infection			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lice infestation			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Acetonaemia			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 1177 (0.08%)	2 / 835 (0.24%)	1 / 1069 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Feeding disorder of infancy or early childhood			
subjects affected / exposed	1 / 1177 (0.08%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 1177 (0.00%)	0 / 835 (0.00%)	0 / 1069 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Flu-control_0.5	Non-Flu-control (TBE/Men C Vaccine)	Non-Flu-control (TBE vaccine)
Total subjects affected by serious adverse events			
subjects affected / exposed	65 / 777 (8.37%)	65 / 607 (10.71%)	45 / 422 (10.66%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain tumour operation			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patent ductus arteriosus repair			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toe amputation			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillectomy			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Developmental delay			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbances			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	2 / 777 (0.26%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Child abuse			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 777 (0.00%)	2 / 607 (0.33%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis chronic			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar disorder			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar haemorrhage			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphemia			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abnormal behaviour			

subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Paracentesis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonoscopy			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental exposure			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 777 (0.13%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	2 / 777 (0.26%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug toxicity			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electric shock			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Foot fracture			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineal injury			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture base			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord injury			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic brain injury			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaccination failure			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod bite			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental poisoning			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cyanosis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Acquired epileptic aphasia			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 777 (0.00%)	2 / 607 (0.33%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Febrile convulsion			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Petit mal epilepsy			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphthous stomatitis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malabsorption			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema multiforme			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Henoch-Schonlein purpura			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photosensitivity reaction			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod infestation			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 777 (0.00%)	2 / 607 (0.33%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 777 (0.00%)	3 / 607 (0.49%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 777 (0.13%)	1 / 607 (0.16%)	3 / 422 (0.71%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter infection			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	3 / 777 (0.39%)	8 / 607 (1.32%)	2 / 422 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 8	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 777 (0.00%)	3 / 607 (0.49%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 777 (0.00%)	2 / 607 (0.33%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	40 / 777 (5.15%)	33 / 607 (5.44%)	31 / 422 (7.35%)
occurrences causally related to treatment / all	0 / 41	1 / 34	0 / 34
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 777 (0.13%)	3 / 607 (0.49%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal infection			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 777 (0.39%)	2 / 607 (0.33%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudocroup			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsilitis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotavirus infection			
subjects affected / exposed	0 / 777 (0.00%)	1 / 607 (0.16%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lice infestation			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			

subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Acetonaemia			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 777 (0.13%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Feeding disorder of infancy or early childhood			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 777 (0.00%)	0 / 607 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	TIV-adj_0.25	TIV-adj_0.5	Flu-control_0.25
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1101 / 1177 (93.54%)	769 / 835 (92.10%)	989 / 1069 (92.52%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 1177 (0.51%)	201 / 835 (24.07%)	6 / 1069 (0.56%)
occurrences (all)	6	303	9
Somnolence			
subjects affected / exposed	381 / 1177 (32.37%)	1 / 835 (0.12%)	315 / 1069 (29.47%)
occurrences (all)	550	1	424
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	77 / 1177 (6.54%)	131 / 835 (15.69%)	69 / 1069 (6.45%)
occurrences (all)	94	158	82
Crying			
alternative assessment type: Systematic			
subjects affected / exposed	390 / 1177 (33.14%)	5 / 835 (0.60%)	349 / 1069 (32.65%)
occurrences (all)	609	5	552
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 1177 (0.08%)	338 / 835 (40.48%)	2 / 1069 (0.19%)
occurrences (all)	1	494	2
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	423 / 1177 (35.94%)	321 / 835 (38.44%)	325 / 1069 (30.40%)
occurrences (all)	612	463	450
Injection site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	146 / 1177 (12.40%)	131 / 835 (15.69%)	107 / 1069 (10.01%)
occurrences (all)	174	149	120
Injection site induration			
alternative assessment type: Systematic			

subjects affected / exposed	214 / 1177 (18.18%)	169 / 835 (20.24%)	131 / 1069 (12.25%)
occurrences (all)	273	211	155
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	334 / 1177 (28.38%)	478 / 835 (57.25%)	250 / 1069 (23.39%)
occurrences (all)	454	747	354
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	123 / 1177 (10.45%)	156 / 835 (18.68%)	90 / 1069 (8.42%)
occurrences (all)	144	190	112
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 1177 (0.00%)	196 / 835 (23.47%)	1 / 1069 (0.09%)
occurrences (all)	0	244	1
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	482 / 1177 (40.95%)	299 / 835 (35.81%)	412 / 1069 (38.54%)
occurrences (all)	750	437	606
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	309 / 1177 (26.25%)	45 / 835 (5.39%)	260 / 1069 (24.32%)
occurrences (all)	434	50	378
Enteritis			
subjects affected / exposed	54 / 1177 (4.59%)	23 / 835 (2.75%)	60 / 1069 (5.61%)
occurrences (all)	61	27	78
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	188 / 1177 (15.97%)	64 / 835 (7.66%)	166 / 1069 (15.53%)
occurrences (all)	240	73	211
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	246 / 1177 (20.90%)	176 / 835 (21.08%)	210 / 1069 (19.64%)
occurrences (all)	331	242	273
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	76 / 1177 (6.46%)	4 / 835 (0.48%)	62 / 1069 (5.80%)
occurrences (all)	88	4	95
Hyperhidrosis			
subjects affected / exposed	1 / 1177 (0.08%)	69 / 835 (8.26%)	1 / 1069 (0.09%)
occurrences (all)	1	85	1
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	327 / 1177 (27.78%)	3 / 835 (0.36%)	263 / 1069 (24.60%)
occurrences (all)	457	4	363
Irritability			
subjects affected / exposed	394 / 1177 (33.47%)	8 / 835 (0.96%)	358 / 1069 (33.49%)
occurrences (all)	645	8	590
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 1177 (0.08%)	85 / 835 (10.18%)	1 / 1069 (0.09%)
occurrences (all)	1	99	1
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 1177 (0.00%)	183 / 835 (21.92%)	0 / 1069 (0.00%)
occurrences (all)	0	243	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	164 / 1177 (13.93%)	83 / 835 (9.94%)	156 / 1069 (14.59%)
occurrences (all)	207	93	186
Bronchitis			
subjects affected / exposed	169 / 1177 (14.36%)	68 / 835 (8.14%)	153 / 1069 (14.31%)
occurrences (all)	229	86	203
Ear infection			
subjects affected / exposed	131 / 1177 (11.13%)	57 / 835 (6.83%)	132 / 1069 (12.35%)
occurrences (all)	207	71	202

Gastroenteritis			
subjects affected / exposed	178 / 1177 (15.12%)	75 / 835 (8.98%)	152 / 1069 (14.22%)
occurrences (all)	211	87	190
Nasopharyngitis			
subjects affected / exposed	153 / 1177 (13.00%)	78 / 835 (9.34%)	161 / 1069 (15.06%)
occurrences (all)	226	102	202
Otitis media			
subjects affected / exposed	250 / 1177 (21.24%)	109 / 835 (13.05%)	226 / 1069 (21.14%)
occurrences (all)	372	132	328
Respiratory tract infection			
subjects affected / exposed	76 / 1177 (6.46%)	29 / 835 (3.47%)	62 / 1069 (5.80%)
occurrences (all)	136	44	122
Rhinitis			
subjects affected / exposed	260 / 1177 (22.09%)	122 / 835 (14.61%)	219 / 1069 (20.49%)
occurrences (all)	315	146	276
Tonsillitis			
subjects affected / exposed	64 / 1177 (5.44%)	38 / 835 (4.55%)	42 / 1069 (3.93%)
occurrences (all)	77	48	45
Upper respiratory tract infection			
subjects affected / exposed	362 / 1177 (30.76%)	170 / 835 (20.36%)	306 / 1069 (28.62%)
occurrences (all)	550	237	525
Viral infection			
subjects affected / exposed	63 / 1177 (5.35%)	35 / 835 (4.19%)	60 / 1069 (5.61%)
occurrences (all)	87	42	80

Non-serious adverse events	Flu-control_0.5	Non-Flu-control (TBE/Men C Vaccine)	Non-Flu-control (TBE vaccine)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	686 / 777 (88.29%)	567 / 607 (93.41%)	375 / 422 (88.86%)
Nervous system disorders			
Headache			
subjects affected / exposed	120 / 777 (15.44%)	5 / 607 (0.82%)	66 / 422 (15.64%)
occurrences (all)	150	5	88
Somnolence			
subjects affected / exposed	1 / 777 (0.13%)	186 / 607 (30.64%)	0 / 422 (0.00%)
occurrences (all)	1	274	0

General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 777 (6.56%)	50 / 607 (8.24%)	37 / 422 (8.77%)
occurrences (all)	55	59	41
Crying			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 777 (0.39%)	178 / 607 (29.32%)	0 / 422 (0.00%)
occurrences (all)	3	277	0
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	224 / 777 (28.83%)	2 / 607 (0.33%)	122 / 422 (28.91%)
occurrences (all)	325	2	168
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	268 / 777 (34.49%)	240 / 607 (39.54%)	128 / 422 (30.33%)
occurrences (all)	375	377	197
Injection site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	93 / 777 (11.97%)	69 / 607 (11.37%)	49 / 422 (11.61%)
occurrences (all)	105	86	61
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	152 / 777 (19.56%)	154 / 607 (25.37%)	79 / 422 (18.72%)
occurrences (all)	199	239	115
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	360 / 777 (46.33%)	173 / 607 (28.50%)	179 / 422 (42.42%)
occurrences (all)	536	250	280
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	128 / 777 (16.47%)	83 / 607 (13.67%)	54 / 422 (12.80%)
occurrences (all)	169	113	72
Malaise			
alternative assessment type:			

Systematic			
subjects affected / exposed	120 / 777 (15.44%)	0 / 607 (0.00%)	64 / 422 (15.17%)
occurrences (all)	154	0	75
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	183 / 777 (23.55%)	221 / 607 (36.41%)	125 / 422 (29.62%)
occurrences (all)	246	334	165
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 777 (4.50%)	147 / 607 (24.22%)	10 / 422 (2.37%)
occurrences (all)	41	219	11
Enteritis			
subjects affected / exposed	18 / 777 (2.32%)	33 / 607 (5.44%)	11 / 422 (2.61%)
occurrences (all)	20	42	12
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	70 / 777 (9.01%)	102 / 607 (16.80%)	23 / 422 (5.45%)
occurrences (all)	77	122	26
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	166 / 777 (21.36%)	119 / 607 (19.60%)	97 / 422 (22.99%)
occurrences (all)	233	147	125
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	5 / 777 (0.64%)	40 / 607 (6.59%)	2 / 422 (0.47%)
occurrences (all)	5	46	2
Hyperhidrosis			
subjects affected / exposed	42 / 777 (5.41%)	1 / 607 (0.16%)	31 / 422 (7.35%)
occurrences (all)	45	1	35
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	1 / 777 (0.13%)	161 / 607 (26.52%)	2 / 422 (0.47%)
occurrences (all)	1	227	2
Irritability			

subjects affected / exposed	6 / 777 (0.77%)	192 / 607 (31.63%)	4 / 422 (0.95%)
occurrences (all)	6	309	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	39 / 777 (5.02%)	1 / 607 (0.16%)	26 / 422 (6.16%)
occurrences (all)	50	1	31
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	102 / 777 (13.13%)	1 / 607 (0.16%)	66 / 422 (15.64%)
occurrences (all)	126	1	82
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	65 / 777 (8.37%)	91 / 607 (14.99%)	45 / 422 (10.66%)
occurrences (all)	72	106	50
Bronchitis			
subjects affected / exposed	66 / 777 (8.49%)	95 / 607 (15.65%)	50 / 422 (11.85%)
occurrences (all)	91	122	63
Ear infection			
subjects affected / exposed	49 / 777 (6.31%)	72 / 607 (11.86%)	22 / 422 (5.21%)
occurrences (all)	65	113	27
Gastroenteritis			
subjects affected / exposed	85 / 777 (10.94%)	94 / 607 (15.49%)	36 / 422 (8.53%)
occurrences (all)	96	110	37
Nasopharyngitis			
subjects affected / exposed	74 / 777 (9.52%)	89 / 607 (14.66%)	36 / 422 (8.53%)
occurrences (all)	95	105	47
Otitis media			
subjects affected / exposed	110 / 777 (14.16%)	130 / 607 (21.42%)	62 / 422 (14.69%)
occurrences (all)	146	211	90
Respiratory tract infection			
subjects affected / exposed	37 / 777 (4.76%)	44 / 607 (7.25%)	17 / 422 (4.03%)
occurrences (all)	66	75	20
Rhinitis			

subjects affected / exposed	97 / 777 (12.48%)	123 / 607 (20.26%)	57 / 422 (13.51%)
occurrences (all)	109	157	63
Tonsillitis			
subjects affected / exposed	38 / 777 (4.89%)	25 / 607 (4.12%)	25 / 422 (5.92%)
occurrences (all)	49	27	32
Upper respiratory tract infection			
subjects affected / exposed	156 / 777 (20.08%)	174 / 607 (28.67%)	85 / 422 (20.14%)
occurrences (all)	212	272	105
Viral infection			
subjects affected / exposed	28 / 777 (3.60%)	20 / 607 (3.29%)	19 / 422 (4.50%)
occurrences (all)	33	26	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 September 2007	Change in the co-coordinating investigator
12 March 2008	The trial V70P5 was started late (in November 2007) during which there was a very high risk of influenza circulation; therefore the enrollment of subjects was stopped prematurely in January 2008 resulting in a low sample size (about 650 subjects). In order to reach the target sample size of 4400 subjects, the protocol was amended to start the enrollment before the start of influenza season 2008/09 in new study sites using a Spring/Fall vaccination schedule. The safety follow-up for the subjects enrolled in this season was extended to 12 months after the vaccination for recording serious adverse events, new onset chronic diseases, and concomitant medications to treat these events
15 July 2008	The study was now considered to be carried out in two parts: Part I (influenza season 2007/08) and Part II (influenza season 2008/09). The trial was planned to be restarted during early fall 2008 in Germany and Finland (influenza season 2008/09) to evaluate efficacy, safety and immunogenicity (in a subgroup) of two vaccines doses, administered following the conventional vaccination schedule, 4 weeks apart. Secondary efficacy endpoints were to be evaluated in enrolled subjects only and the household members were not to be included in the trial for the evaluation of indirect vaccine efficacy. Cell mediated immune responses were not to be explored. Influsplit SSW (also marketed with the brand name of Fluarix, GlaxoSmithKline) (NH composition 2008/09) split influenza vaccine was to be administered during the second year of the trial (influenza season 2008/09) as flu vaccine comparator. The planned overall sample size was increased (5500 subjects) and children were to be enrolled and randomized in a 2:2:1 ratio to one of the three vaccine groups [FLUAD (2200 subjects): Influsplit SSW (2200 subjects):Menjugate/Encepur children (overall 1100 subjects)]; As secondary efficacy endpoints to be evaluated during the second year of the study (influenza season 2008/09) Fluad vaccine efficacy relative to the split flu vaccine control has been added.
17 October 2008	Administrative changes

19 May 2009	The study was extended to include third consecutive influenza season 2009/10 and approximately 3500 unprimed healthy children aged 6 to < 36 months were planned to be enrolled. The 6 to <36 month-old subjects were to be randomly allocated in a 2:2:1 ratio, to one of the three vaccine groups (TIV-adj (Fluad), or Influsplit SSW, or menjugate/Encepur Children). Each subject was to receive intramuscularly, depending on the assigned vaccine, two 0.25mL doses of either Fluad or Influsplit SSW, or two 0.5mL doses of Menjugate (if 6 to <12 months of age), or two 0.25mL doses of Encepur Children (if ≥12 months of age). During Part III of the study a subset of approximately 550 children were to be enrolled, in selected study centers, for the immunogenicity evaluation. The primary end points were to demonstrate the safety and tolerability of TIV-adj compared with Flu-control, and the clinical protection provided by TIV-adj, compared with Non-flu control, in unprimed children aged 6 to <36 months. The safety and tolerability, as well as the clinical protection provided by TIV-adj in the whole age population (6 to <72 months) was to be evaluated as secondary study end points. An interim analysis was planned on data for all local and systemic reactions and all adverse events recorded during Part I of the study (influenza season 2007/2008) and for all local and systemic reactions and all adverse events recorded up to three weeks after second vaccination in all subjects enrolled during Part II of the study (influenza season 2008/2009). This interim analysis was to be performed, before start of the Part III of the study, by an independent safety Data Monitoring Committee (DMC). Details on the statistical methods to analyze the primary efficacy endpoints and primary safety endpoint have been added
10 June 2009	In order to provide the subjects who were randomized to Menjugate/Encepur Children vaccines during Part III of the study (2009/10 Influenza season) with a third dose, an additional follow up clinic visit was added to the study design, to comply with the current SPC of the vaccines. This additional follow up clinic visit was to occur after the unblinding of Part III of the study (i.e. after the study visit/telephone call scheduled at day 181 or at the end of the influenza surveillance period, whichever was longer).
27 July 2009	In order to provide the subjects who were randomized to Menjugate/Encepur Children vaccines during Part III of the study (2009/10 Influenza season) with a third dose, an additional follow up clinic visit was added to the study design, to comply with the current SPC of the vaccines. This additional follow up clinic visit was to occur after the unblinding of Part III of the study (i.e. after the study visit/telephone call scheduled at day 181 or at the end of the influenza surveillance period, whichever was longer). Subjects were to be offered the H1N1sw vaccine (Focetria (H1N1sw) or FCC (H1N1sw) that has been assigned to their country, only in the dose and formulation that was regulatory approved for their age. These vaccinations were completely voluntary, however, if the vaccines were not approved and available within the timelines of the trial (before Day 181), the trial was to end without these additional vaccines administered. If subjects had access to a competitor H1N1sw vaccine that was approved and available before the Novartis H1N1sw vaccines, they were to follow the H1N1 visit schedule to assess the safety of the competitor vaccine. ILI symptoms and swabs would be collected from Visit 1 till the End of Study Secondary absolute efficacy objectives were amended to include the evaluation of the number of a) all-cause hospitalizations, b) hospitalizations due to confirmed influenza, c) all-cause outpatient medical visits and d) outpatient medical visits due to influenza illness or influenza symptoms in view of the 2009-2010 H1N1 swine pandemic caused by a novel influenza A (H1N1) virus of swine origin. As well as the potential for vaccination against this pandemic strain in unprimed children aged 6 to <36 months, if adequate data is available. Data regarding the booster doses of Non-flu control vaccine (Menjugate® /Encephur®Children) in the season 2009/10 will not be presented as an addendum to this CSR.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/21995388