Clinical trial results:
A Randomized, Open Label, Single Center, Dose- and Regimen-Ranging Study to Evaluate Immunogenicity, Safety and Tolerability of Different Formulations of an Adjuvanted and Non-Adjuvanted Egg-Derived, Inactivated Novel Swine Origin A/H1N1 Monovalent Subunit Influenza Virus Vaccine in Healthy Children and Adults Ages 3 to 64 Years

Summary

EudraCT number	2014-005185-30
Trial protocol	Outside EU/EEA
Global end of trial date	12 October 2010
Results information	
Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	30 April 2015
Version creation reason	• Correction of full data set Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required. Moreover, a change in system user for this study is necessary.

Trial information

Trial identification	
Sponsor protocol code	V112_04
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00973700
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	350 Massachusetts Ave, Cambridge, MA, United States, 02139
Public contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.com

Notes:

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 March 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 October 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate vaccine 15mcg a/H1N1 S-OIV unadjuvanted hemagglutination inhibition (HI) assay results in the adult and pooled pediatric populations according to immunogenicity criteria defined by CBER recommendations.

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Regulatory reason
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Costa Rica: 784
Worldwide total number of subjects	784
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	257

Adolescents (12-17 years)	135
Adults (18-64 years)	392
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at one center in Costa Rica.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	2x7.5adj

Arm description:

A/H1N1 7.5 mcg with MF59; two doses on day 1

Arm type	Experimental
Investigational medicinal product name	Monovalent H1N1 influenza virus vaccine with MF59 adjuvant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 0.5 mL was administered in each arm.

Arm title	7.5adj_1_8

Arm description:

A/H1N1 7.5 mcg with MF59; one dose on days 1 and 8

Arm type	Experimental
Investigational medicinal product name	Monovalent H1N1 influenza virus vaccine with MF59 adjuvant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL / dose

Arm title	7.5adj_1_22

Arm description:

A/H1N1 7.5 mcg with MF59; one dose on days 1 and 22

Arm type	Experimental
Investigational medicinal product name	Monovalent H1N1 influenza virus vaccine with MF59 adjuvant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL / dose

Arm title	15_1_22
Arm description:	
A/H1N1 15 mcg no MF59; one dose on days 1 and 22	
Arm type	Experimental
Investigational medicinal product name	Monovalent H1N1 influenza virus vaccine without MF59 adjuvant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL / dose	

Arm title	2x15_1_22
Arm description:	
A/H1N1 15 mcg no MF59; two doses on days 1 and 22	
Arm type	Experimental
Investigational medicinal product name	Monovalent H1N1 influenza virus vaccine without MF59 adjuvant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose of 0.25 mL was administered in each arm.	

Number of subjects in period 1	2x7.5adj	7.5adj_1_8	7.5adj_1_22
Started	56	56	168
Completed	49	54	158
Not completed	7	2	10
Consent withdrawn by subject	2	2	8
Inappropriate enrollment	-	-	-
Unable to classify	-	-	1
Lost to follow-up	5	-	1

Number of subjects in period 1	15_1_22	2x15_1_22
Started	336	168
Completed	318	158
Not completed	18	10
Consent withdrawn by subject	4	4
Inappropriate enrollment	4	-
Unable to classify	2	1
Lost to follow-up	8	5

Baseline characteristics

Reporting groups	
Reporting group title	2x7.5adj
Reporting group description:	
A/H1N1 7.5 mcg with MF59; two doses on day 1	
Reporting group title	7.5adj_1_8
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 8	
Reporting group title	7.5adj_1_22
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 22	
Reporting group title	15_1_22
Reporting group description:	
A/H1N1 15 mcg no MF59; one dose on days 1 and 22	
Reporting group title	2x15_1_22
Reporting group description:	
A/H1N1 15 mcg no MF59; two doses on days 1 and 22	

Reporting group values	2x7.5adj	7.5adj_1_8	7.5adj_1_22
Number of subjects	56	56	168
Age categorical Units: Subjects			
3 to <9 years	0	0	56
9 to 17 years	0	0	56
18 to 64 years	56	56	56
Gender categorical Units: Subjects			
Female (3 to <9 years)	0	0	29
Male (3 to <9 years)	0	0	27
Female (9 to 17 years)	0	0	40
Male (9 to 17 years)	0	0	16
Female (18 to 64 years)	33	40	29
Male (18 to 64 years)	23	16	27

Reporting group values	15_1_22	2x15_1_22	Total
Number of subjects	336	168	784
Age categorical Units: Subjects			
3 to <9 years	84	56	196
9 to 17 years	84	56	196
18 to 64 years	168	56	392
Gender categorical Units: Subjects			
Female (3 to <9 years)	46	23	98
Male (3 to <9 years)	38	33	98
Female (9 to 17 years)	40	30	110
Male (9 to 17 years)	44	26	86
Female (18 to 64 years)	96	29	227

Male (18 to 64 years)	72	27	165

End points

End points reporting groups

Reporting group title	2x7.5adj
Reporting group description:	
A/H1N1 7.5 mcg with MF59; two doses on day 1	
Reporting group title	7.5adj_1_8
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 8	
Reporting group title	7.5adj_1_22
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 22	
Reporting group title	15_1_22
Reporting group description:	
A/H1N1 15 mcg no MF59; one dose on days 1 and 22	
Reporting group title	2x15_1_22
Reporting group description:	
A/H1N1 15 mcg no MF59; two doses on days 1 and 22	
Subject analysis set title	Per protocol set (3 to <9 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects included in the full analysis set (FAS), who received all the relevant doses of vaccine correctly, provided evaluable serum samples at relevant time points and had no major protocol violations as pre-specified in analysis plan prior to unblinding.	
Subject analysis set title	As Enrolled set (3 to <9 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects (3 to <9 years) enrolled in this study.	
Subject analysis set title	Per protocol set (9 to 17 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects included in the FAS, who received all the relevant doses of vaccine correctly, provided evaluable serum samples at relevant time points and had no major protocol violations as pre-specified in analysis plan prior to unblinding.	
Subject analysis set title	As Enrolled set (9 to 17 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects (9 to 17 years) enrolled in this study.	
Subject analysis set title	Safety set (3 to <9 years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who actually received a study vaccination and provided post-baseline safety data.	
Subject analysis set title	Per protocol set (18 to 64 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects included in the FAS, who received all the relevant doses of vaccine correctly, provided evaluable serum samples at relevant time points and had no major protocol violations as pre-specified in analysis plan prior to unblinding.	
Subject analysis set title	Safety set (18 to 64 years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who actually received a study vaccination and provided post-baseline safety data	

Subject analysis set title	Safety set (9 to 17 years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who actually received a study vaccination and provided post-baseline safety data.	
Subject analysis set title	As Enrolled set (18 to 64 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects (18 to 64 years) enrolled in this study.	

Primary: 1. Percentage of Subjects With Seroconversion and HI Titer ≥1:40 in Children 3 to 17 Years of Age.

End point title	1. Percentage of Subjects With Seroconversion and HI Titer ≥1:40 in Children 3 to 17 Years of Age.[1][2]
End point description:	
Seroconversion: The percentage of subjects with either a pre-vaccination HI titer < 1:10 and a post-vaccination HI titer >1:40 or a prevaccination HI titer >1:10 and a minimum four-fold rise in post-vaccination HI antibody titer. The analyses were performed on the Per-Protocol Set (PPS).	
End point type	Primary
End point timeframe:	
Day 1 to day 387	

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

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point

End point values	15_1_22			
Subject group type	Reporting group			
Number of subjects analysed	149			
Units: Percentages of subjects				
number (confidence interval 95%)				
HI Titer ≥40 on day 1	26 (19 to 33)			
HI Titer ≥40 on day 22	83 (76 to 89)			
HI Titer ≥40 on day 29	95 (91 to 98)			
HI Titer ≥40 on day 43	92 (86 to 96)			
HI Titer ≥40 on day 217 (N=129)	88 (81 to 93)			
HI Titer ≥40 on day 387 (N=136)	80 (72 to 86)			
Seroconversion on day 22	79 (71 to 85)			
Seroconversion on day 29	92 (86 to 96)			
Seroconversion on day 43	87 (81 to 92)			
Seroconversion on day 217 (N=129)	71 (62 to 78)			
Seroconversion on day 387 (N=136)	63 (54 to 71)			

Statistical analyses

No statistical analyses for this end point

Primary: 2. Percentage of Subjects With Seroconversion and HI Titer ≥1:40 in Adults 18 to 64 Years of Age.

End point title	2. Percentage of Subjects With Seroconversion and HI Titer ≥1:40 in Adults 18 to 64 Years of Age.[3][4]

End point description:

Seroconversion: The percentage of subjects with either a pre-vaccination HI titer < 1:10 and a post-vaccination HI titer >1:40 or a prevaccination HI titer >1:10 and a minimum four-fold rise in post-vaccination HI antibody titer. The analyses were performed on the Per-Protocol Set (PPS).

End point type	Primary

End point timeframe:

Day 1 to day 387

Notes:

[3] - 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

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point

End point values	15_1_22			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Percentages of subjects				
number (confidence interval 95%)				
HI Titer ≥40 on day 1	18 (12 to 26)			
HI Titer ≥40 on day 8	93 (87 to 97)			
HI Titer ≥40 on day 15	99 (96 to 100)			
HI Titer ≥40 on day 22	98 (95 to 100)			
HI Titer ≥40 on day 29	99 (96 to 100)			
HI Titer ≥40 on day 43	100 (97 to 100)			
HI Titer ≥40 on day 217 (N=111)	91 (84 to 96)			
HI Titer ≥40 on day 387 (N=120)	84 (76 to 90)			
Seroconversion on day 8	86 (78 to 91)			
Seroconversion on day 15	94 (88 to 97)			
Seroconversion on day 22	94 (88 to 97)			
Seroconversion on day 29	95 (90 to 98)			
Seroconversion on day 43	95 (90 to 98)			
Seroconversion on day 217 (N=111)	81 (73 to 88)			
Seroconversion on day 387 (N=120)	75 (66 to 82)			

Statistical analyses

No statistical analyses for this end point

Secondary: 3. Percentage of Subjects With Seroconversion and HI Titer ≥1:40, in 3 to <9 Years and 9 to 17 Years.

End point title	3. Percentage of Subjects With Seroconversion and HI Titer ≥1:40, in 3 to <9 Years and 9 to 17 Years.[5]

End point description:

Seroconversion: The percentage of subjects with either a pre-vaccination HI titer < 1:10 and a post-vaccination HI titer >1:40 or a prevaccination HI titer >1:10 and a minimum four-fold rise in post-vaccination HI antibody titer. The analyses were performed on the PPS.

End point type	Secondary

End point timeframe:

Day 1 to day 387

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point

End point values	7.5adj_1_22	15_1_22	2x15_1_22	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	75	47	
Units: Percentages of subjects				
number (confidence interval 95%)				
HI Titer ≥40 on day 1 (3 to <9 yrs)	24 (13 to 39)	23 (14 to 34)	23 (12 to 38)	
HI Titer ≥40 on day 22 (3 to <9 yrs)	93 (82 to 99)	71 (59 to 81)	79 (64 to 89)	
HI Titer ≥40 on day 29 (3 to <9 yrs)	100 (92 to 100)	92 (83 to 97)	96 (85 to 99)	
HI Titer ≥40 on day 43 (3 to <9 yrs)	100 (92 to 100)	85 (75 to 92)	96 (85 to 99)	
HI Titer ≥40 on day 217 (3 to <9 yrs; N=41,66,40)	100 (91 to 100)	80 (69 to 89)	78 (62 to 89)	
HI Titer ≥40 on day 387 (3 to <9 yrs; N=43,70,42)	93 (81 to 99)	73 (61 to 83)	62 (46 to 76)	
Seroconversion on day 22 (3 to <9 yrs)	91 (79 to 98)	69 (58 to 79)	79 (64 to 89)	
Seroconversion on day 29 (3 to <9 yrs)	98 (88 to 100)	92 (83 to 97)	96 (85 to 99)	
Seroconversion on day 43 (3 to <9 yrs)	96 (85 to 99)	84 (74 to 91)	94 (82 to 99)	
Seroconversion on day 217 (3 to <9 yrs;N=41,66,40)	88 (74 to 96)	65 (52 to 76)	65 (48 to 79)	
Seroconversion on day 387 (3 to <9 yrs;N=43,70,42	77 (61 to 88)	56 (43 to 68)	50 (34 to 66)	
HI Titer ≥40 on day 1 (9 to 17 yrs; N=45,74,52)	42 (28 to 58)	28 (19 to 40)	33 (20 to 47)	
HI Titer ≥40 on day 22 (9 to 17 yrs; N=45,74,52)	98 (88 to 100)	96 (89 to 99)	100 (93 to 100)	
HI Titer ≥40 on day 29 (9 to 17 yrs; N=45,74,52)	100 (92 to 100)	99 (93 to 100)	100 (93 to 100)	
HI Titer ≥40 on day 43 (9 to 17 yrs; N=45,74,52)	100 (92 to 100)	99 (93 to 100)	100 (93 to 100)	
HI Titer ≥40 on day 217 (9 to 17 yrs; N=37,63,45)	100 (91 to 100)	95 (87 to 99)	98 (88 to 100)	
HI Titer ≥40 on day 387 (9 to 17 yrs; N=37,66,47)	89 (75 to 97)	88 (78 to 95)	89 (77 to 96)	
Seroconversion on day 22 (9 to 17 yrs; N=45,74,52)	87 (73 to 95)	88 (78 to 94)	94 (84 to 99)	
Seroconversion on day 29 (9 to 17 yrs; N=45,74,52)	89 (76 to 96)	92 (83 to 97)	94 (84 to 99)	
Seroconversion on day 43 (9 to 17 yrs; N=45,74,52)	84 (71 to 94)	98 (89 to 100)	92 (81 to 98)	
Seroconversion on day 217 (9 to 17 yrs;N=37,63,45)	68 (50 to 82)	76 (64 to 86)	76 (60 to 87)	
Seroconversion on day 387 (9 to 17 yrs;N=37,66,47)	59 (42 to 75)	70 (57 to 80)	70 (55 to 83)	

Statistical analyses

No statistical analyses for this end point

Secondary: 4. HI GMRs, in 3 to <9 Years and 9 to 17 Years.

End point title	4. HI GMRs, in 3 to <9 Years and 9 to 17 Years.[6]

End point description:

Geometric Mean Ratios (GMRs) of HI antibody assay (ratio of post-vaccination versus pre-vaccination HI titers). The analyses were performed on the PPS.

End point type	Secondary

End point timeframe:

Day 1 to day 387

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point

End point values	7.5adj_1_22	15_1_22	2x15_1_22	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	75	47	
Units: Ratio				
geometric mean (confidence interval 95%)				
GMR on day 22 (3 to <9 yrs)	31 (19 to 50)	12 (8.51 to 18)	16 (10 to 26)	
GMR on day 29 (3 to <9 yrs)	169 (110 to 260)	35 (25 to 49)	53 (35 to 82)	
GMR on day 43 (3 to <9 yrs)	120 (75 to 192)	22 (15 to 32)	44 (27 to 69)	
GMR on day 217 (3 to <9 yrs; N=41,66,40)	19 (12 to 30)	7.79 (5.46 to 11)	8.07 (5.11 to 13)	
GMR on day 387 (3 to <9 yrs; N=43,70,42)	14 (8.27 to 24)	6.9 (4.58 to 10)	5.94 (3.5 to 10)	
GMR on day 22 (9 to 17 yrs; N=45,74,52)	42 (24 to 74)	52 (34 to 81)	66 (39 to 111)	
GMR on day 29 (9 to 17 yrs; N=45,74,52)	63 (36 to 109)	70 (45 to 108)	79 (47 to 132)	
GMR on day 43 (9 to 17 yrs; N=45,74,52)	44 (25 to 77)	48 (31 to 75)	59 (35 to 100)	
GMR on day 217 (9 to 17 yrs; N=37,63,45)	10 (5.66 to 18)	17 (11 to 26)	13 (7.92 to 23)	
GMR on day 387 (9 to 17 yrs; N=37,66,47)	7.22 (3.77 to 14)	16 (9.53 to 25)	13 (7.53 to 24)	

Statistical analyses

No statistical analyses for this end point

Secondary: 5. HI GMRs, in adults 18 to 64 Years.

End point title	5. HI GMRs, in adults 18 to 64 Years.

End point description:

Geometric Mean Ratios (GMRs) of HI antibody assay (ratio of post-vaccination versus pre-vaccination HI titers). The analyses were performed on the PPS.

End point type	Secondary

End point timeframe:

Day 1 to day 387

End point values	2x7.5adj	7.5adj_1_8	7.5adj_1_22	15_1_22
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	45	45	132
Units: Ratio				
geometric mean (confidence interval 95%)				
GMR on day 8	48 (28 to 85)	35 (21 to 60)	57 (33 to 97)	43 (32 to 59)
GMR on day 15	115 (70 to 189)	181 (113 to 292)	200 (124 to 322)	138 (104 to 182)
GMR on day 22	79 (48 to 130)	100 (63 to 160)	123 (77 to 197)	85 (64 to 111)
GMR on day 29	56 (35 to 89)	76 (49 to 118)	160 (103 to 248)	83 (64 to 107)
GMR on day 43	44 (27 to 71)	64 (40 to 101)	101 (63 to 161)	76 (58 to 100)
GMR on day 217 (N=0,0,35,111,34)	0 (0 to 0)	0 (0 to 0)	30 (18 to 48)	16 (12 to 20)
GMR on day 387 (N=38,40,38,120,42)	6.61 (3.92 to 11)	11 (6.81 to 19)	21 (12 to 36)	12 (8.99 to 16)

End point values	2x15_1_22			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: Ratio				
geometric mean (confidence interval 95%)				
GMR on day 8	63 (37 to 106)			
GMR on day 15	123 (77 to 197)			
GMR on day 22	72 (45 to 113)			
GMR on day 29	66 (43 to 101)			
GMR on day 43	65 (41 to 102)			
GMR on day 217 (N=0,0,35,111,34)	16 (10 to 27)			
GMR on day 387 (N=38,40,38,120,42)	9.21 (5.61 to 15)			

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Percentage of Subjects With Seroconversion and HI Titer ≥1:40, in Adults 18 to 64 Years.

End point title	6. Percentage of Subjects With Seroconversion and HI Titer ≥1:40, in Adults 18 to 64 Years.

End point description:

Seroconversion: The percentage of subjects with either a pre-vaccination HI titer < 1:10 and a post-vaccination HI titer >1:40 or a prevaccination HI titer >1:10 and a minimum four-fold rise in post-

vaccination HI antibody titer. The analyses were performed on the PPS.

End point type	Secondary
End point timeframe:	
Day 1 to day 387	

End point values	2x7.5adj	7.5adj_1_8	7.5adj_1_22	15_1_22
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	45	45	132
Units: Percentages of subjects				
number (confidence interval 95%)				
HI Titer ≥40 on day 1	20 (9 to 35)	22 (11 to 37)	13 (5 to 27)	18 (12 to 26)
HI Titer ≥40 on day 8	100 (91 to 100)	91 (79 to 98)	96 (85 to 99)	93 (87 to 97)
HI Titer ≥40 on day 15	100 (91 to 100)	100 (92 to 100)	98 (88 to 100)	99 (96 to 100)
HI Titer ≥40 on day 22	100 (91 to 100)	98 (88 to 100)	98 (88 to 100)	98 (95 to 100)
HI Titer ≥40 on day 29	100 (91 to 100)	98 (88 to 100)	100 (92 to 100)	99 (96 to 100)
HI Titer ≥40 on day 43	98 (87 to 100)	100 (92 to 100)	98 (88 to 100)	100 (97 to 100)
HI Titer ≥40 on day 217 (N=0,0,35,111,34)	0 (0 to 0)	0 (0 to 0)	97 (85 to 100)	91 (84 to 96)
HI Titer ≥40 on day 387 (N=38,40,38,120,42)	76 (60 to 89)	90 (76 to 97)	92 (79 to 98)	84 (76 to 90)
Seroconversion on day 8	95 (83 to 99)	80 (65 to 90)	93 (82 to 99)	86 (78 to 91)
Seroconversion on day 15	98 (87 to 100)	100 (92 to 100)	98 (88 to 100)	94 (88 to 97)
Seroconversion on day 22	95 (83 to 99)	91 (79 to 98)	96 (85 to 99)	94 (88 to 97)
Seroconversion on day 29	95 (83 to 99)	93 (82 to 99)	98 (88 to 100)	95 (90 to 98)
Seroconversion on day 43	85 (71 to 94)	93 (82 to 99)	96 (85 to 99)	95 (90 to 98)
Seroconversion on day 217 (N=0,0,35,111,34)	0 (0 to 0)	0 (0 to 0)	94 (81 to 99)	81 (73 to 88)
Seroconversion on day 387 (N=38,40,38,120,42)	66 (49 to 80)	80 (64 to 91)	87 (72 to 96)	75 (66 to 82)

End point values	2x15_1_22			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: Percentages of subjects				
number (confidence interval 95%)				
HI Titer ≥40 on day 1	21 (11 to 36)			
HI Titer ≥40 on day 8	96 (85 to 99)			
HI Titer ≥40 on day 15	100 (92 to 100)			
HI Titer ≥40 on day 22	98 (89 to 100)			
HI Titer ≥40 on day 29	100 (92 to 100)			
HI Titer ≥40 on day 43	100 (92 to 100)			

HI Titer ≥40 on day 217 (N=0,0,35,111,34)	97 (85 to 100)			
HI Titer ≥40 on day 387 (N=38,40,38,120,42)	83 (69 to 93)			
Seroconversion on day 8	94 (82 to 99)			
Seroconversion on day 15	98 (89 to 100)			
Seroconversion on day 22	96 (85 to 99)			
Seroconversion on day 29	98 (89 to 100)			
Seroconversion on day 43	98 (89 to 100)			
Seroconversion on day 217 (N=0,0,35,111,34)	88 (73 to 97)			
Seroconversion on day 387 (N=38,40,38,120,42)	69 (53 to 82)			

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Number of Subjects With at Least One Reactogenicity Sign, in 3 to <9 Years of Age.

End point title	7. Number of Subjects With at Least One Reactogenicity Sign, in 3 to <9 Years of Age.[7]

End point description:

Number of subjects with specified solicited local and systemic reactions in adult subjects (3 to <9 years of age). Postvac: postvaccination Analges: analgesics Antipyr: antipyretics The analyses were performed on the safety set.
Note: 1) postvac 1 = after the first vaccination and 2) postvac 2 = after the second vaccination

End point type	Secondary

End point timeframe:

7 days after each vaccination

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point

End point values	7.5adj_1_22	15_1_22	2x15_1_22	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	84	54	
Units: Number of subjects				
Local Reactions postvac. 1	25	31	20	
Erythema postvac. 1	1	0	0	
Induration postvac. 1	0	3	1	
Swelling postvac. 1	3	4	3	
Tenderness postvac. 1	21	23	17	
Pain postvac. 1	21	25	17	
Systemic Reaction postvac. 1	24	28	17	
Headache postvac. 1	7	12	9	
Fatigue postvac. 1	6	8	5	
Myalgia postvac. 1	4	8	6	
Arthralgia postvac. 1	0	2	2	
Chills postvac. 1	3	1	2	

Nausea postvac. 1	5	7	4	
Vomiting postvac. 1	0	1	2	
Diarrhea postvac. 1	0	0	1	
Other Reactions postvac. 1	10	10	6	
Analges/Antipyr Used postvac. 1 (N=55,83,54)	9	8	6	
Stayed Home postvac. 1 (N=55,83,54)	1	2	0	
Body Temp > 40 C postvac. 1	0	0	0	
Local Reactions postvac. 2 (N=55,83,54)	20	29	21	
Erythema postvac. 2 (N=55,83,54)	3	1	1	
Induration postvac. 2 (N=55,83,54)	8	1	2	
Swelling postvac. 2 (N=55,83,54)	8	0	2	
Tenderness postvac. 2 (N=55, 83, 54)	15	27	16	
Pain postvac. 2 (N=55,83,54)	18	23	19	
Systemic Reaction postvac. 2 (N=55,83,54)	13	22	18	
Headache postvac. 2 (N=55,83,54)	5	12	3	
Fatigue postvac. 2 (N=55,83,54)	1	5	2	
Myalgia postvac. 2 (N=55,83,54)	3	2	5	
Arthralgia postvac. 2 (N=55,83,54)	0	2	5	
Chills postvac. 2 (N=55,83,54)	2	2	1	
Nausea postvac. 2 (N=55,83,54)	5	5	1	
Vomiting postvac. 2 (N=55,83,54)	0	1	3	
Diarrhea postvac. 2 (N=55,83,54)	0	1	2	
Other Reactions postvac. 2 (N=55,83,54)	5	7	7	
Analges/Antipyr Used postvac. 2 (N=55,83,54)	4	6	7	
Stayed Home postvac. 2 (N=55,82,54)	1	2	0	
Body Temp > 40 C postvac. 2 (N=55,83,54)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Number of Subjects With at Least One Reactogenicity Sign, in 9 to 17 Years of Age.

End point title	8. Number of Subjects With at Least One Reactogenicity Sign, in 9 to 17 Years of Age.[8]

End point description:

Number of subjects with specified solicited local and systemic reactions in adult subjects (9 to 17 years of age). Postvac: postvaccination Analges: analgesics Antipyr: antipyretics The analyses were performed on the safety set.
Note: 1) postvac 1 = after the first vaccination and 2) postvac 2 = after the second vaccination.

End point type	Secondary

End point timeframe:

7 days after each vaccination

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point

End point values	7.5adj_1_22	15_1_22	2x15_1_22	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	84	57	
Units: Number of subjects				
Local Reactions postvac. 1	37	36	29	
Erythema postvac. 1	1	1	0	
Induration postvac. 1	1	6	1	
Swelling postvac. 1	1	4	3	
Tenderness postvac. 1	26	23	21	
Pain postvac. 1	32	30	25	
Systemic Reaction postvac. 1	24	36	16	
Headache postvac. 1	17	20	8	
Fatigue postvac. 1	9	13	11	
Myalgia postvac. 1	11	15	11	
Arthralgia postvac. 1	2	2	0	
Chills postvac. 1	1	2	1	
Nausea postvac. 1	3	7	5	
Vomiting postvac. 1	0	1	0	
Diarrhea postvac. 1	2	0	0	
Other Reactions postvac. 1	11	10	8	
Analges/Antipyr Used postvac. 1	10	10	7	
Stayed Home postvac. 1	2	1	2	
Body Temp > 40 C postvac. 1	0	0	0	
Local Reactions postvac. 2 (N=52,84,55)	31	36	27	
Erythema postvac. 2 (N=52,84,55)	0	3	1	
Induration postvac. 2 (N=52,84,55)	2	3	4	
Swelling postvac. 2 (N=52,84,55)	2	5	3	
Tenderness postvac. 2 (N=52,84, 55)	20	25	25	
Pain postvac. 2 (N=52,84,55)	27	30	26	
Systemic Reaction postvac. 2 (N=52,84,55)	18	29	14	
Headache postvac. 2 (N=52,84,55)	12	16	8	
Fatigue postvac. 2 (N=52,84,55)	3	6	9	
Myalgia postvac. 2 (N=52,84,55)	8	9	7	
Arthralgia postvac. 2 (N=52,84,55)	0	4	4	
Chills postvac. 2 (N=52,84,55)	2	2	3	
Nausea postvac. 2 (N=52,84,55)	3	7	2	
Vomiting postvac. 2 (N=52,84,55)	1	0	0	
Diarrhea postvac. 2 (N=52,84,55)	2	3	0	
Other Reactions postvac. 2 (N=52,84,55)	1	10	4	
Analges/Antipyr Used postvac. 2 (N=52,84,55)	1	9	4	
Stayed Home postvac. 2 (N=52,84,55)	0	1	0	
Body Temp > 40 C postvac. 2 (N=52,84,55)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of Subjects With at Least One Reactogenicity Sign, in 18 to 64 Years of Age.

End point title	9. Number of Subjects With at Least One Reactogenicity Sign, in 18 to 64 Years of Age.

End point description:

Number of subjects with specified solicited local and systemic reactions in adult subjects (18 to 64 years of age). Postvac: postvaccination Analges: analgesics Antipyr: antipyretics The analyses were performed on the safety set.
Note: 1) postvac 1 = after the first vaccination and 2) postvac 2 = after the second vaccination

End point type	Secondary

End point timeframe:

7 days after each vaccination

End point values	2x7.5adj	7.5adj_1_8	7.5adj_1_22	15_1_22
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	56	56	159
Units: Number of subjects				
Local Reactions postvac. 1	39	26	38	56
Erythema postvac. 1	3	0	2	2
Induration postvac. 1	5	4	5	6
Swelling postvac. 1	3	3	5	4
Tenderness postvac. 1	33	21	26	35
Pain postvac. 1	36	23	32	41
Systemic Reaction postvac. 1	34	31	31	71
Headache postvac. 1	26	18	22	42
Fatigue postvac. 1	17	16	16	32
Myalgia postvac. 1	21	13	16	28
Arthralgia postvac. 1	4	1	6	10
Chills postvac. 1	4	3	6	6
Nausea postvac. 1	7	9	8	16
Vomiting postvac. 1	0	0	0	1
Diarrhea postvac. 1	2	1	0	8
Other Reactions postvac. 1	14	7	12	13
Analges/Antipyr Used postvac. 1	14	6	12	13
Stayed Home postvac. 1 (N=53,55,56,157,54)	2	1	2	0
Body Temp > 40 C postvac. 1	0	0	0	0
Local Reactions postvac. 2 (N=0,55,56,158,53)	0	21	28	56
Erythema postvac. 2 (N=0,55,56,158,53)	0	1	2	5
Induration postvac. 2 (N=0,55,56,158,53)	0	3	4	4
Swelling postvac. 2 (N=0,55,56,158,53)	0	2	5	7
Tenderness postvac. 2 (N=0,55,56,158,53)	0	16	24	48
Pain postvac. 2 (N=0,55,56,158,53)	0	19	24	45
Systemic Reaction postvac. 2 (N=0,55,56,158,53)	0	26	28	53

Headache postvac. 2 (N=0,55,56,158,53)	0	18	18	25
Fatigue postvac. 2 (N=0,55,56,158,53)	0	14	13	24
Myalgia postvac. 2 (N=0,55,56,158,53	0	9	14	26
Arthralgia postvac. 2 (N=0,55,56,158,53)	0	5	7	16
Chills postvac. 2 (N=0,55,56,158,53)	0	8	5	5
Nausea postvac. 2 (N=0,55,56,158,53)	0	8	5	7
Vomiting postvac. 2 (N=0,55,56,158,53)	0	1	0	2
Diarrhea postvac. 2 (N=0,55,56,158,53)	0	1	0	4
Other Reactions postvac. 2 (N=0,55,56,158,53)	0	8	7	11
Analges/Antipyr Used postvac. 2 (N=0,55,56,158,53)	0	7	7	11
Stayed Home postvac. 2 (N=0,55,56,158,53)	0	2	0	1
Body Temp > 40 C postvac. 2 (N=0,55,56,158,53)	0	0	0	1

End point values	2x15_1_22			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: Number of subjects				
Local Reactions postvac. 1	19			
Erythema postvac. 1	1			
Induration postvac. 1	3			
Swelling postvac. 1	2			
Tenderness postvac. 1	14			
Pain postvac. 1	16			
Systemic Reaction postvac. 1	22			
Headache postvac. 1	12			
Fatigue postvac. 1	15			
Myalgia postvac. 1	12			
Arthralgia postvac. 1	2			
Chills postvac. 1	4			
Nausea postvac. 1	3			
Vomiting postvac. 1	1			
Diarrhea postvac. 1	3			
Other Reactions postvac. 1	5			
Analges/Antipyr Used postvac. 1	4			
Stayed Home postvac. 1 (N=53,55,56,157,54)	1			
Body Temp > 40 C postvac. 1	0			
Local Reactions postvac. 2 (N=0,55,56,158,53)	17			
Erythema postvac. 2 (N=0,55,56,158,53)	1			
Induration postvac. 2 (N=0,55,56,158,53)	3			
Swelling postvac. 2 (N=0,55,56,158,53)	5			
Tenderness postvac. 2 (N=0,55,56,158,53)	16			

Pain postvac. 2 (N=0,55,56,158,53)	15			
Systemic Reaction postvac. 2 (N=0,55,56,158,53)	14			
Headache postvac. 2 (N=0,55,56,158,53)	11			
Fatigue postvac. 2 (N=0,55,56,158,53)	10			
Myalgia postvac. 2 (N=0,55,56,158,53	7			
Arthralgia postvac. 2 (N=0,55,56,158,53)	4			
Chills postvac. 2 (N=0,55,56,158,53)	8			
Nausea postvac. 2 (N=0,55,56,158,53)	3			
Vomiting postvac. 2 (N=0,55,56,158,53)	1			
Diarrhea postvac. 2 (N=0,55,56,158,53)	1			
Other Reactions postvac. 2 (N=0,55,56,158,53)	7			
Analges/Antipyr Used postvac. 2 (N=0,55,56,158,53)	6			
Stayed Home postvac. 2 (N=0,55,56,158,53)	2			
Body Temp > 40 C postvac. 2 (N=0,55,56,158,53)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) and serious adverse events (SAEs) were collected throughout the duration of the study (day 1 to day 387).

Adverse event reporting additional description:

Data provided in Other Adverse Events (>5%) were collected. The data included solicited local and systemic reactions that persisted for more than 7 days after each study vaccination. The number of participants at risk is not the same with the numbers provided in the participant flow module as these numbers are analyzed by age and group.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	2x7.5adj (18 to 64 Yrs)
Reporting group description:	
A/H1N1 7.5 mcg with MF59; two doses on day 1	
Reporting group title	7.5adj_1_8 (18 to 64 Yrs)
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 8	
Reporting group title	7.5adj_1_22 (18 to 64 Yrs)
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 22	
Reporting group title	15_1_22 (18 to 64 Yrs)
Reporting group description:	
A/H1N1 15 mcg no MF59; one dose on days 1 and 22	
Reporting group title	2x15_1_22 (18 to 64 Yrs)
Reporting group description:	
A/H1N1 15 mcg no MF59; two doses on days 1 and 22	
Reporting group title	7.5adj_1_22 (9 to 17 Yrs)
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 22	
Reporting group title	15_1_22 (9 to 17 Yrs)
Reporting group description:	
A/H1N1 15 mcg no MF59; one dose on days 1 and 22	
Reporting group title	2x15_1_22 (9 to 17 Yrs)
Reporting group description:	
A/H1N1 15 mcg no MF59; two doses on days 1 and 22	
Reporting group title	7.5adj_1_22 (3 to <9 Yrs)
Reporting group description:	
A/H1N1 7.5 mcg with MF59; one dose on days 1 and 22	
Reporting group title	15_1_22 (3 to <9 Yrs)
Reporting group description:	
A/H1N1 15 mcg no MF59; one dose on days 1 and 22	
Reporting group title	2x15_1_22 (3 to <9 Yrs)
Reporting group description:	
A/H1N1 15 mcg no MF59; two doses on days 1 and 22	

Serious adverse events	2x7.5adj (18 to 64 Yrs)	7.5adj_1_8 (18 to 64 Yrs)	7.5adj_1_22 (18 to 64 Yrs)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 54 (3.70%)	0 / 56 (0.00%)	1 / 56 (1.79%)
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 / 54 (0.00%)	0 / 56 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 54 (1.85%)	0 / 56 (0.00%)	0 / 56 (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			
Hysterectomy			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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 repair			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Rhinoplasty			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			
subjects affected / exposed	1 / 54 (1.85%)	0 / 56 (0.00%)	0 / 56 (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

High risk pregnancy			
subjects affected / exposed	1 / 54 (1.85%)	0 / 56 (0.00%)	0 / 56 (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
Social circumstances			
Sexual abuse			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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			
Uterine haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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			
Precocious puberty			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (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	1 / 54 (1.85%)	0 / 56 (0.00%)	0 / 56 (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

Serious adverse events	15_1_22 (18 to 64 Yrs)	2x15_1_22 (18 to 64 Yrs)	7.5adj_1_22 (9 to 17 Yrs)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 159 (2.52%)	1 / 54 (1.85%)	1 / 53 (1.89%)
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 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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
Breast cancer			
subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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			
Hysterectomy			
subjects affected / exposed	1 / 159 (0.63%)	0 / 54 (0.00%)	0 / 53 (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
Inguinal hernia repair			
subjects affected / exposed	1 / 159 (0.63%)	0 / 54 (0.00%)	0 / 53 (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
Rhinoplasty			

subjects affected / exposed	0 / 159 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			
subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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
High risk pregnancy			
subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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			
Sexual abuse			
subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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	0 / 159 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
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			
Uterine haemorrhage			
subjects affected / exposed	1 / 159 (0.63%)	0 / 54 (0.00%)	0 / 53 (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			
Nephrolithiasis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 54 (0.00%)	0 / 53 (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			
Precocious puberty			

subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 159 (0.63%)	0 / 54 (0.00%)	0 / 53 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (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	15_1_22 (9 to 17 Yrs)	2x15_1_22 (9 to 17 Yrs)	7.5adj_1_22 (3 to <9 Yrs)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 84 (1.19%)	0 / 57 (0.00%)	2 / 55 (3.64%)
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 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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
Breast cancer			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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			
Hysterectomy			

subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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 repair			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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
Rhinoplasty			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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
High risk pregnancy			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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			
Sexual abuse			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	1 / 55 (1.82%)
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 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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			
Uterine haemorrhage			

subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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			
Precocious puberty			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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 / 84 (1.19%)	0 / 57 (0.00%)	0 / 55 (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
Urinary tract infection			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (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	15_1_22 (3 to <9 Yrs)	2x15_1_22 (3 to <9 Yrs)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Brain neoplasm			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hysterectomy			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia repair			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinoplasty			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
High risk pregnancy			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Sexual abuse			

subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Precocious puberty			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	2x7.5adj (18 to 64 Yrs)	7.5adj_1_8 (18 to 64 Yrs)	7.5adj_1_22 (18 to 64 Yrs)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 54 (90.74%)	41 / 56 (73.21%)	48 / 56 (85.71%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 54 (1.85%)	3 / 56 (5.36%)	1 / 56 (1.79%)
occurrences (all)	1	3	1
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 54 (50.00%)	21 / 56 (37.50%)	27 / 56 (48.21%)
occurrences (all)	31	49	57
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 54 (7.41%)	9 / 56 (16.07%)	8 / 56 (14.29%)
occurrences (all)	5	11	12
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 54 (31.48%)	20 / 56 (35.71%)	22 / 56 (39.29%)
occurrences (all)	20	34	36
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 54 (5.56%)	1 / 56 (1.79%)	3 / 56 (5.36%)
occurrences (all)	5	1	4
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	39 / 54 (72.22%)	31 / 56 (55.36%)	42 / 56 (75.00%)
occurrences (all)	130	79	113
Injection site swelling			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 54 (1.85%)	2 / 56 (3.57%)	2 / 56 (3.57%)
occurrences (all)	2	2	2
Pyrexia			
subjects affected / exposed	2 / 54 (3.70%)	4 / 56 (7.14%)	6 / 56 (10.71%)
occurrences (all)	2	5	8
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 54 (3.70%)	2 / 56 (3.57%)	1 / 56 (1.79%)
occurrences (all)	2	4	1
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 54 (12.96%)	13 / 56 (23.21%)	11 / 56 (19.64%)
occurrences (all)	7	23	17
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	1 / 56 (1.79%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 54 (3.70%)	2 / 56 (3.57%)	1 / 56 (1.79%)
occurrences (all)	2	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 54 (7.41%)	6 / 56 (10.71%)	10 / 56 (17.86%)
occurrences (all)	4	6	14
Back pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 56 (1.79%)	3 / 56 (5.36%)
occurrences (all)	0	1	4
Myalgia			
alternative assessment type: Systematic			

subjects affected / exposed	21 / 54 (38.89%)	17 / 56 (30.36%)	22 / 56 (39.29%)
occurrences (all)	28	25	34
Pain in extremity			
subjects affected / exposed	1 / 54 (1.85%)	3 / 56 (5.36%)	2 / 56 (3.57%)
occurrences (all)	1	3	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 54 (18.52%)	6 / 56 (10.71%)	8 / 56 (14.29%)
occurrences (all)	11	7	8
Tonsillitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 54 (1.85%)	2 / 56 (3.57%)	5 / 56 (8.93%)
occurrences (all)	1	2	6
Varicella			
subjects affected / exposed	0 / 54 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	15_1_22 (18 to 64 Yrs)	2x15_1_22 (18 to 64 Yrs)	7.5adj_1_22 (9 to 17 Yrs)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	119 / 159 (74.84%)	35 / 54 (64.81%)	46 / 53 (86.79%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 159 (0.63%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	56 / 159 (35.22%)	17 / 54 (31.48%)	21 / 53 (39.62%)
occurrences (all)	91	30	39
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 159 (6.29%)	11 / 54 (20.37%)	3 / 53 (5.66%)
occurrences (all)	12	14	3
Fatigue			

alternative assessment type: Systematic			
subjects affected / exposed	45 / 159 (28.30%)	18 / 54 (33.33%)	11 / 53 (20.75%)
occurrences (all)	73	30	13
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 159 (3.77%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences (all)	7	3	1
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	79 / 159 (49.69%)	23 / 54 (42.59%)	42 / 53 (79.25%)
occurrences (all)	173	108	116
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 159 (3.14%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences (all)	5	2	1
Pyrexia			
subjects affected / exposed	12 / 159 (7.55%)	2 / 54 (3.70%)	3 / 53 (5.66%)
occurrences (all)	13	2	4
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 159 (8.18%)	3 / 54 (5.56%)	4 / 53 (7.55%)
occurrences (all)	13	5	4
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 159 (13.21%)	5 / 54 (9.26%)	6 / 53 (11.32%)
occurrences (all)	28	8	6
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 159 (1.89%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	5	2	1
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	8 / 159 (5.03%)	3 / 54 (5.56%)	0 / 53 (0.00%)
occurrences (all)	9	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 159 (15.09%)	4 / 54 (7.41%)	2 / 53 (3.77%)
occurrences (all)	32	7	2
Back pain			
subjects affected / exposed	2 / 159 (1.26%)	2 / 54 (3.70%)	0 / 53 (0.00%)
occurrences (all)	3	3	0
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	42 / 159 (26.42%)	17 / 54 (31.48%)	18 / 53 (33.96%)
occurrences (all)	73	22	22
Pain in extremity			
subjects affected / exposed	1 / 159 (0.63%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	24 / 159 (15.09%)	6 / 54 (11.11%)	7 / 53 (13.21%)
occurrences (all)	26	7	7
Tonsillitis			
subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 159 (3.77%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	7	0	1
Varicella			
subjects affected / exposed	0 / 159 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	15_1_22 (9 to 17 Yrs)	2x15_1_22 (9 to 17 Yrs)	7.5adj_1_22 (3 to <9 Yrs)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 84 (79.76%)	43 / 57 (75.44%)	40 / 55 (72.73%)
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 84 (0.00%)	1 / 57 (1.75%)	0 / 55 (0.00%)
occurrences (all)	0	1	0
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	29 / 84 (34.52%)	11 / 57 (19.30%)	11 / 55 (20.00%)
occurrences (all)	48	22	12
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 84 (4.76%)	4 / 57 (7.02%)	4 / 55 (7.27%)
occurrences (all)	4	5	6
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 84 (17.86%)	14 / 57 (24.56%)	6 / 55 (10.91%)
occurrences (all)	23	26	7
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 84 (4.76%)	1 / 57 (1.75%)	3 / 55 (5.45%)
occurrences (all)	4	1	4
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	52 / 84 (61.90%)	37 / 57 (64.91%)	32 / 55 (58.18%)
occurrences (all)	117	160	75
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 84 (2.38%)	1 / 57 (1.75%)	3 / 55 (5.45%)
occurrences (all)	2	1	3
Pyrexia			
subjects affected / exposed	3 / 84 (3.57%)	6 / 57 (10.53%)	8 / 55 (14.55%)
occurrences (all)	3	8	8
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			

subjects affected / exposed	5 / 84 (5.95%)	0 / 57 (0.00%)	1 / 55 (1.82%)
occurrences (all)	5	0	1
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 84 (14.29%)	6 / 57 (10.53%)	8 / 55 (14.55%)
occurrences (all)	16	11	10
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 84 (3.57%)	1 / 57 (1.75%)	0 / 55 (0.00%)
occurrences (all)	3	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 84 (4.76%)	1 / 57 (1.75%)	0 / 55 (0.00%)
occurrences (all)	4	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 84 (5.95%)	5 / 57 (8.77%)	0 / 55 (0.00%)
occurrences (all)	7	5	0
Back pain			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	20 / 84 (23.81%)	14 / 57 (24.56%)	5 / 55 (9.09%)
occurrences (all)	26	22	8
Pain in extremity			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	0 / 55 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 84 (14.29%)	11 / 57 (19.30%)	4 / 55 (7.27%)
occurrences (all)	15	12	6
Tonsillitis			

subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	3 / 55 (5.45%)
occurrences (all)	0	0	4
Upper respiratory tract infection			
subjects affected / exposed	3 / 84 (3.57%)	3 / 57 (5.26%)	4 / 55 (7.27%)
occurrences (all)	3	3	5
Varicella			
subjects affected / exposed	0 / 84 (0.00%)	0 / 57 (0.00%)	1 / 55 (1.82%)
occurrences (all)	0	0	1

Non-serious adverse events	15_1_22 (3 to <9 Yrs)	2x15_1_22 (3 to <9 Yrs)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 84 (72.62%)	41 / 54 (75.93%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences (all)	0	0	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 84 (25.00%)	11 / 54 (20.37%)	
occurrences (all)	31	15	
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 84 (2.38%)	2 / 54 (3.70%)	
occurrences (all)	3	3	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 84 (13.10%)	6 / 54 (11.11%)	
occurrences (all)	16	9	
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 84 (1.19%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Injection site pain			
alternative assessment type: Systematic			

subjects affected / exposed	43 / 84 (51.19%)	29 / 54 (53.70%)	
occurrences (all)	102	116	
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 84 (2.38%)	2 / 54 (3.70%)	
occurrences (all)	2	2	
Pyrexia			
subjects affected / exposed	10 / 84 (11.90%)	10 / 54 (18.52%)	
occurrences (all)	13	12	
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 84 (3.57%)	5 / 54 (9.26%)	
occurrences (all)	3	5	
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 84 (11.90%)	5 / 54 (9.26%)	
occurrences (all)	14	5	
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 84 (2.38%)	5 / 54 (9.26%)	
occurrences (all)	2	5	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 84 (7.14%)	4 / 54 (7.41%)	
occurrences (all)	7	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 84 (4.76%)	7 / 54 (12.96%)	
occurrences (all)	4	7	
Back pain			
subjects affected / exposed	0 / 84 (0.00%)	0 / 54 (0.00%)	
occurrences (all)	0	0	
Myalgia			

alternative assessment type: Systematic			
subjects affected / exposed	10 / 84 (11.90%)	9 / 54 (16.67%)	
occurrences (all)	12	13	
Pain in extremity			
subjects affected / exposed	1 / 84 (1.19%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	17 / 84 (20.24%)	11 / 54 (20.37%)	
occurrences (all)	20	15	
Tonsillitis			
subjects affected / exposed	3 / 84 (3.57%)	6 / 54 (11.11%)	
occurrences (all)	3	6	
Upper respiratory tract infection			
subjects affected / exposed	7 / 84 (8.33%)	6 / 54 (11.11%)	
occurrences (all)	9	7	
Varicella			
subjects affected / exposed	0 / 84 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2009	- Follow-up extended from 6 months to 12 months after last vaccination. - Addition of children to Cohort E with subsequent increase in sample size from 672 to 784 and shift in randomization ratio in groups C, D, and E from 1:1:0 to 2:3:2. - Vaccine Group E design changed from a single 30 µg dose to 2 x 15 µg doses administered in two locations on Day 1 and Day 22. - Removal of injection site ecchymosis, arthralgia, chills, malaise, and sweating as solicited adverse events. Addition of injection site tenderness, vomiting, and diarrhea as solicited adverse events. - Safety laboratory assessments according to standardized toxicity scales. - Medically attended visits added as a safety endpoint. - Full Analysis Set for interim analyses on Day 8, 15, 22, 29 and 43. - Assent to be performed for individuals ages 10 years and older. - No Diary cards to be completed for individuals under 13 years. - Physical assessment procedures at Visit 1 and subsequent visits defined in greater detail. - Procedures for monthly telephone contacts with subjects from Visit 7 through Visit 16 added. - Exclusion criterion added, to specify subjects who received or intended to receive influenza vaccine within 1 week before or after each study vaccination.

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/21285531