Clinical trial results:
Immunogenicity and Safety of Multiple Formulations of an Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With and Without Adjuvant in Healthy European Subjects Aged 6 to 35 Months

Summary

EudraCT number	2009-013858-32
Trial protocol	FI
Global end of trial date	05 January 2011

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	29 January 2015

Trial information

Trial identification

Sponsor protocol code	GPF09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00956046
WHO universal trial number (UTN)	U1111-1111-5029

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Director, Clinical Development, Sanofi Pasteur SA, 33 4 37 37 58 50, stephanie.pepin@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 4 37 37 58 50, stephanie.pepin@sanofipasteur.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 April 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 January 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To describe the immune response of each candidate vaccine 21 days after each vaccination by hemagglutination inhibition (HAI) and seroneutralization (SN) testing in all subjects.
• To describe the antibody persistence eight months (M8) after the first vaccine administration using HAI method in a subset of subjects who received two half doses of either the 15 µg HA or 3.8 µg HA + AF03 vaccine (amendment 2).
• To describe the safety profiles (injection site reactions and systemic events) of each candidate vaccine during the 21 days following each vaccination, and serious adverse events throughout the study in all subjects
•To describe the immune response against the A/H1N1 strain using the HAI method 21 days after last vaccination with the 2010-2011 NH seasonal TIV administered 13 months after the first vaccination in a subset of subjects who received two half-doses of either the 15 µg HA or 3.8 µg HA + AF03 A/H1N1 influenza vaccines as primary series (amendment 3).

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

The non-adjuvanted formulation was chosen based on Sanofi Pasteur experience with seasonal influenza vaccine (Vaxigrip).

Actual start date of recruitment	16 September 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 401
Worldwide total number of subjects	401
EEA total number of subjects	401

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)	253
Children (2-11 years)	148
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:

Study subjects were enrolled from 16 September 2009 to 07 October 2009 in 15 clinical centers in Finland.

Pre-assignment

Screening details:

A total of 401 subjects who met all inclusion criteria and none of the exclusion criteria were enrolled and vaccinated.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	1.9 µg HA + ½ AF03; 6-11 months

Arm description:

Subjects aged 6-11 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.

Arm type	Experimental
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated, adjuvanted with AF03)
Investigational medicinal product code	452
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.25 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Arm title	3.8 µg HA + ½ AF03; 6-11 months

Arm description:

Subjects aged 6-11 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.

Arm type	Experimental
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated, adjuvanted with AF03)
Investigational medicinal product code	452
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.25 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Arm title	3.8 µg HA + AF03; 6-11 months

Arm description:

Subjects aged 6-11 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.

Arm type	Experimental
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated, adjuvanted with AF03)
Investigational medicinal product code	452
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Arm title	7.5 µg HA; 6-11 months

Arm description:

Subjects aged 6-11 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.

Arm type	Active comparator
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated)
Investigational medicinal product code	448
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.25 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Arm title	1.9 µg HA + ½ AF03; 12-35 months

Arm description:

Subjects aged 12-35 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.

Arm type	Experimental
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated, adjuvanted with AF03)
Investigational medicinal product code	452
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.25 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Arm title	3.8 µg HA + ½ AF03; 12-35 months

Arm description:

Subjects aged 12-35 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.

Arm type	Experimental
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated, adjuvanted with AF03)
Investigational medicinal product code	452
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.25 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Arm title	3.8 µg HA + AF03; 12-35 months

Arm description:

Subjects aged 12-35 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza

vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.

Arm type	Experimental
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated, adjuvanted with AF03)
Investigational medicinal product code	452
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Arm title	7.5 µg HA; 12-35 months

Arm description:

Subjects aged 12-35 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.

Arm type	Active comparator
Investigational medicinal product name	Swine A/H1N1 Influenza Vaccine (split virion, inactivated)
Investigational medicinal product code	448
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.25 mL dose, intramuscular into the deltoid (subjects ≥1 year of age) or thigh (subjects <1 year of age), two doses 21 days apart.

Number of subjects in period 1	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months
Started	48	50	52
Completed	46	46	48
Not completed	2	4	4
Consent withdrawn by subject	1	1	2
Adverse event, non-fatal	1	1	-
Protocol deviation	-	2	2

Number of subjects in period 1	7.5 µg HA; 6-11 months	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months
Started	51	48	50
Completed	50	48	50
Not completed	1	0	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Started	52	50
Completed	51	48
Not completed	1	2

Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	1
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	1.9 µg HA + ½ AF03; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + ½ AF03; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + AF03; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.	
Reporting group title	7.5 µg HA; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.	
Reporting group title	1.9 µg HA + ½ AF03; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + ½ AF03; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + AF03; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.	
Reporting group title	7.5 µg HA; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.	

Reporting group values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months
Number of subjects	48	50	52
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	48	50	52
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0

Age continuous Units: months			
arithmetic mean	9.4	9	8.9
standard deviation	± 1.5	± 1.7	± 1.9
Gender categorical Units: Subjects			
Female	25	27	25
Male	23	23	27
Influenza vaccination 2008/2009 Units: Subjects			
Yes	0	0	0
No	44	47	48
Unknown	0	0	0
Not applicable	4	3	4
Influenza vaccination 2007/2008 Units: Subjects			
Yes	0	0	0
No	0	1	0
Unknown	0	0	0
Not applicable	48	49	52
Influenza vaccination 2006/2007 Units: Subjects			
Yes	0	0	0
No	0	0	0
Uknown	0	0	0
Not applicable	48	50	52
Experience influenza infection during the 2008/2009 season Units: Subjects			
Yes	0	0	0
No	47	50	52
Unknown	1	0	0
Subject in contact with a confirmed and/or probable case of H1N1 within 8 months prior to enrollment Units: Subjects			
Yes	0	2	0
No	48	47	52
Unknown	0	1	0

Reporting group values	7.5 µg HA; 6-11 months	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months
Number of subjects	51	48	50
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	51	13	15
Children (2-11 years)	0	35	35
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	9.1	27.3	26.3
standard deviation	± 1.4	± 6.4	± 6.3
Gender categorical Units: Subjects			
Female	27	22	24
Male	24	26	26
Influenza vaccination 2008/2009 Units: Subjects			
Yes	0	24	27
No	50	21	20
Unknown	0	3	3
Not applicable	1	0	0
Influenza vaccination 2007/2008 Units: Subjects			
Yes	0	17	18
No	0	21	23
Unknown	0	2	2
Not applicable	51	8	7
Influenza vaccination 2006/2007 Units: Subjects			
Yes	0	1	0
No	0	15	15
Uknown	0	1	0
Not applicable	51	31	35
Experience influenza infection during the 2008/2009 season Units: Subjects			
Yes	1	1	1
No	49	44	48
Unknown	1	3	1
Subject in contact with a confirmed and/or probable case of H1N1 within 8 months prior to enrollment Units: Subjects			
Yes	0	0	0
No	51	47	49
Unknown	0	1	1

Reporting group values	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months	Total
Number of subjects	52	50	401
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	14	10	253
Children (2-11 years)	38	40	148
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	27.6	27.1	
standard deviation	± 6.4	± 5.9	-
Gender categorical Units: Subjects			
Female	28	21	199
Male	24	29	202
Influenza vaccination 2008/2009 Units: Subjects			
Yes	31	26	108
No	20	24	274
Unknown	1	0	7
Not applicable	0	0	12
Influenza vaccination 2007/2008 Units: Subjects			
Yes	20	21	76
No	25	22	92
Unknown	0	0	4
Not applicable	7	7	229
Influenza vaccination 2006/2007 Units: Subjects			
Yes	0	0	1
No	21	15	66
Uknown	0	0	1
Not applicable	31	35	333
Experience influenza infection during the 2008/2009 season Units: Subjects			
Yes	1	2	6
No	49	46	385
Unknown	2	2	10
Subject in contact with a confirmed and/or probable case of H1N1 within 8 months prior to enrollment Units: Subjects			
Yes	0	0	2
No	52	49	395
Unknown	0	1	4

End points

End points reporting groups

Reporting group title	1.9 µg HA + ½ AF03; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + ½ AF03; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + AF03; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.	
Reporting group title	7.5 µg HA; 6-11 months
Reporting group description:	
Subjects aged 6-11 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.	
Reporting group title	1.9 µg HA + ½ AF03; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + ½ AF03; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.	
Reporting group title	3.8 µg HA + AF03; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.	
Reporting group title	7.5 µg HA; 12-35 months
Reporting group description:	
Subjects aged 12-35 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.	

Primary: Geometric Mean Titers (GMTs) of Antibody Assayed by HAI Method Against A/California (H1N1) Strain in Subjects Age 6 to 11 Months After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers (GMTs) of Antibody Assayed by HAI Method Against A/California (H1N1) Strain in Subjects Age 6 to 11 Months After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[1][2]
End point description:	
Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method.	
End point type	Primary
End point timeframe:	
Day 0 (pre-vaccination) and Day 21 and Day 42 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)
Day 21	200 (154 to 259)	256 (204 to 322)	290 (238 to 354)	18.4 (14.1 to 24)
Day 42	3008 (2474 to 3656)	2500 (2102 to 2974)	3241 (2777 to 3783)	184 (142 to 239)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Antibody Assayed by HAI Method Against A/California (H1N1) Strain in Subjects Age 12-35 Months After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers (GMTs) of Antibody Assayed by HAI Method Against A/California (H1N1) Strain in Subjects Age 12-35 Months After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[3][4]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	5.04 (4.96 to 5.11)	5.21 (4.79 to 5.67)	5 (5 to 5)	5 (5 to 5)
Day 21	253 (191 to 337)	220 (170 to 285)	409 (334 to 502)	28.3 (19.8 to 40.4)
Day 42	2736 (2221 to 3370)	2524 (2143 to 2973)	3748 (3212 to 4374)	244 (174 to 342)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 6-Months with Antibody Titers ≥ 40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 6-Months with Antibody Titers ≥ 40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[5][6]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[5] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	0	0	0
Day 21	95.7	97.9	100	32.7
Day 42	100	100	100	98

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 12-35 Months with Antibody Titers ≥40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 12-35 Months with Antibody Titers ≥40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain After Vaccination with Intramuscular Inactivated, Split-virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[7][8]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[7] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	2	0	0
Day 21	97.8	98	100	34
Day 42	100	100	100	97.9

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 6-11 Months Achieving Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 6-11 Months Achieving

	Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[9][10]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method. Seroconversion was defined as subjects with pre-vaccination titer <10 (1/dil) on Day 0, post-vaccination titer ≥40 (1/dil) or significant increase for subjects with pre-vaccination titer ≥10 (1/dil), ≥4-fold increase of the titer after vaccination (post/pre).

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-vaccination

Notes:

[9] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[10] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Percentage of subjects				
number (not applicable)				
Day 21	95.7	97.9	100	32.7
Day 42	100	100	100	98

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 12-35 Months Achieving Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 12-35 Months Achieving Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[11][12]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method. Seroconversion was defined as subjects with pre-vaccination titer <10 (1/dil) on Day 0, post-vaccination titer ≥40 (1/dil) or significant increase for subjects with pre-vaccination titer ≥10 (1/dil), ≥4-fold increase of the titer after vaccination (post/pre).

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-vaccination

Notes:

[11] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[12] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Percentage of subjects				
number (not applicable)				
Day 21	97.8	98	100	34
Day 42	100	100	100	97.9

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 6 to 11 Months with Neutralizing Antibody Titers ≥40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 6 to 11 Months with Neutralizing Antibody Titers ≥40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[13][14]

End point description:

Immunogenicity was evaluated using the seroneutralization method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[13] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[14] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Percentage of subjects				
number (not applicable)				

Day 0	0	0	0	0
Day 21	97.9	100	97.8	69.4
Day 42	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 12-35 Months with Neutralizing Antibody Titers ≥ 40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 12-35 Months with Neutralizing Antibody Titers ≥ 40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[15][16]

End point description:

Immunogenicity was evaluated using the seroneutralization method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[15] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[16] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	0	1.9	0
Day 21	100	98	100	76.6
Day 42	100	100	100	97.9

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Age 6-11 Months After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Age 6-11 Months After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[17][18]

End point description:

Immunogenicity was evaluated using the seroneutralization method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[17] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[18] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	5.18 (4.82 to 5.57)	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)
Day 21	817 (583 to 1146)	1196 (918 to 1558)	1179 (849 to 1636)	56.4 (39.1 to 81.3)
Day 42	9546 (9085 to 10031)	9214 (8526 to 9956)	9969 (9612 to 10340)	1035 (780 to 1372)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Age 12-35 Months After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Age 12-35 Months After Intramuscular Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[19][20]

End point description:

Immunogenicity was evaluated using the seroneutralization method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[19] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[20] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	5.09 (4.91 to 5.28)	5 (5 to 5)	5.25 (4.76 to 5.8)	5 (5 to 5)
Day 21	1113 (853 to 1452)	981 (712 to 1351)	1875 (1491 to 2358)	95.1 (59.8 to 151)
Day 42	8539 (7617 to 9571)	9158 (8450 to 9926)	9761 (9185 to 10372)	1170 (791 to 1730)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 6-11 Months with 2- and 4-fold Increase in Neutralizing Antibody Titers Assayed by Seroneutralization Against A/California (H1N1) Strain After Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 6-11 Months with 2- and 4-fold Increase in Neutralizing Antibody Titers Assayed by Seroneutralization Against A/California (H1N1) Strain After Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[21][22]

End point description:

Immunogenicity was evaluated using the seroneutralization method.

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-vaccination

Notes:

[21] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[22] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Percentage of subjects				
number (not applicable)				
≥2-fold increase from Day 0; Day 21	97.9	100	97.8	89.8
≥2-fold increase from Day 0; Day 42	100	100	100	100
≥4-fold increase from Day 0; Day 21	97.9	100	97.8	77.6
≥4-fold increase from Day 0; Day 42	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 12-35 Months with 2- and 4-fold Increase in Neutralizing Antibody Titers Assayed by Seroneutralization Against A/California (H1N1) Strain After Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 12-35 Months with 2- and 4-fold Increase in Neutralizing Antibody Titers Assayed by Seroneutralization Against A/California (H1N1) Strain After Inactivated, Split-virion A/H1N1 Influenza Vaccine With or Without Adjuvant[23][24]

End point description:

Immunogenicity was evaluated using the seroneutralization method.

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-vaccination

Notes:

[23] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[24] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Percentage of subjects				
number (not applicable)				
≥2-fold increase from Day 0; Day 21	100	98	100	89.4
≥2-fold increase from Day 0; Day 42	100	100	100	100
≥4-fold increase from Day 0; Day 21	100	98	100	85.1
≥4-fold increase from Day 0; Day 42	100	100	100	97.9

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Antibody Assayed by SRH Method Against A/California (H1N1) Strain in Subjects Age 6 to 11 Months Old Before and After Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers (GMTs) of Antibody Assayed by SRH Method Against A/California (H1N1) Strain in Subjects Age 6 to 11 Months Old Before and After Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[25][26]

End point description:

Immunogenicity was evaluated using Single radial hemolysis (SRH) testing.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[25] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[26] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Titers (mm2)				
geometric mean (confidence interval 95%)				
Day 0	4.53 (4.07 to 5.05)	4.32 (3.95 to 4.72)	4.71 (4.19 to 5.3)	4.67 (4.13 to 5.27)
Day 21	75 (67.9 to 82.8)	77.3 (70.8 to 84.5)	78.6 (72.2 to 85.6)	33.1 (29.6 to 37.1)
Day 42	115 (110 to 121)	111 (106 to 116)	116 (112 to 121)	53.5 (49.1 to 58.2)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers of Antibody Assayed by SRH Against A/California

(H1N1) Strain in Subjects Age 12-35 Months Before and After Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers of Antibody Assayed by SRH Against A/California (H1N1) Strain in Subjects Age 12-35 Months Before and After Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[27][28]

End point description:

Immunogenicity was evaluated using Single radial hemolysis (SRH) testing.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[27] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[28] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Titers (mm2)				
geometric mean (confidence interval 95%)				
Day 0	5.23 (4.4 to 6.21)	6.18 (5.13 to 7.44)	6.45 (5.31 to 7.83)	5.35 (4.41 to 6.49)
Day 21	83.9 (77.5 to 90.8)	77.1 (68.6 to 86.7)	96.3 (89.5 to 104)	43.2 (36.4 to 51.3)
Day 42	119 (115 to 124)	112 (107 to 118)	124 (121 to 128)	61 (52.8 to 70.4)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 6 to 11 Months Old With Seroprotection Against A/California (H1N1) Strain Following Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 6 to 11 Months Old With Seroprotection Against A/California (H1N1) Strain Following Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[29][30]

End point description:

Immunogenicity was evaluated using Single radial hemolysis (SRH) testing. Seroprotection was defined as titers ≥25 mm² on Day 0, Day 21 and Day 42.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[29] - 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: Descriptive analyses were performed based on the age group specified.

[30] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	0	0	0
Day 21	97.9	97.9	100	77.6
Day 42	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 12 to 35 Months Old With Seroprotection Against A/California (H1N1) Strain Following Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 12 to 35 Months Old With Seroprotection Against A/California (H1N1) Strain Following Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[31][32]

End point description:

Immunogenicity was evaluated using Single radial hemolysis (SRH) testing. Seroprotection was defined as titers ≥25 mm² on Day 0, Day 21 and Day 42.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 and Day 42 post-vaccination

Notes:

[31] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[32] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Percentage of subjects				
number (not applicable)				
Day 0	2.1	0	5.8	4
Day 21	100	98	100	78.7
Day 42	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 12 to 35 Months Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 12 to 35 Months Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[33][34]

End point description:

Solicited inj. site: Tenderness (<24 mths)/Pain (≥24 mths), Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions (<24 mths): Fever, Vomiting, Crying abnormal, Drowsiness, Appetite loss, Irritability. Solicited systemic reactions (≥24 mths): Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 Solicited inj. site reactions: Tenderness–Cries when injected limb is moved or the movement is reduced; Pain–Incapacitating, prevents performance of usual activities; Erythema, Swelling, Induration, and Ecchymosis–≥5 cm. Grade 3 Solicited systemic reactions (<24 mths): Fever–>39.5°C; Vomiting–≥6 episodes/24 hours or requiring parenteral hydration; Crying abnormal - >3 hours; Drowsiness–Sleeping most of the time or difficult to wake; Appetite loss–Refusing ≥3 feeds/meals or refusing most feeds/meals; Irritability–Inconsolable. Grade 3 Solicited systemic reactions (≥24 mths): Fever–≥39.0°C; Headache, Malaise, Myalgia, and Shivering–Significant, prevents daily activity.

End point type	Primary

End point timeframe:

Day 0 up to Day 7 post-any vaccination

Notes:

[33] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[34] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	50
Units: Percentage of subjects				
number (not applicable)				
Inj. site Pain/Tenderness	58.3	56	55.8	38.8

Grade 3 Inj. site Pain/Tenderness	0	0	3.8	0
Inj. site Erythema	37.5	32	53.8	24.5
Grade 3 Inj. site Erythema	4.2	6	9.6	0
Inj. site Swelling	14.6	12	23.1	14.3
Grade 3 Inj. site Swelling	4.2	4	5.8	0
Inj. site Induration	20.8	30	19.2	10.2
Grade 3 Inj. site Induration	0	0	1.9	2
Inj. site Ecchymosis	12.5	28	9.6	16.3
Grade 3 Inj. site Ecchymosis	0	0	0	0
Vomiting	7.1	13.3	0	0
Grade 3 Vomiting	0	0	0	0
Crying abnormal	28.6	46.7	53.3	50
Grade 3 Crying abnormal	0	0	6.7	10
Drowsiness	28.6	26.7	40	40
Grade 3 Drowsiness	0	0	0	10
Appetite lost	50	60	73.3	40
Grade 3 Appetite lost	0	0	13.3	10
Irritability	35.7	60	66.7	60
Grade 3 Irritability	0	13.3	6.7	20
Headache	8.8	2.9	5.4	5.1
Grade 3 Headache	0	0	0	0
Malaise	29.4	8.6	10.8	25.6
Grade 3 Malaise	14.7	0	0	2.6
Myalgia	26.5	14.3	24.3	12.8
Grade 3 Myalgia	2.9	0	0	0
Fever; 12 to 23 months	28.6	20	26.7	20
Grade 3 Fever; 12 to 23 months	14.3	0	0	0
Fever; 24 to 35 months	11.8	17.1	21.6	5.1
Grade 3 Fever; 24 to 35 months	2.9	2.9	0	0
Shivering	17.6	2.9	24.3	2.6
Grade 3 Shivering	2.9	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 6 to 11 Months Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 6 to 11 Months Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Intramuscular Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[35][36]

End point description:

Solicited inj. site: Tenderness (<24 mths)/Pain (≥24 mths), Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions (<24 mths): Fever, Vomiting, Crying abnormal, Drowsiness, Appetite loss, Irritability. Solicited systemic reactions (≥24 mths): Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 Solicited inj. site reactions: Tenderness–Cries when injected limb is moved or the movement is reduced; Pain–Incapacitating, prevents performance of usual activities; Erythema, Swelling, Induration, and Ecchymosis–≥5 cm. Grade 3 Solicited systemic reactions (<24 mths): Fever–>39.5°C; Vomiting–≥6 episodes/24 hours or requiring parenteral hydration; Crying abnormal -

hours; Drowsiness–Sleeping most of the time or difficult to wake; Appetite loss–Refusing ≥3 feeds/meals or refusing most feeds/meals; Irritability–Inconsolable. Grade 3 Solicited systemic reactions (≥24 mths): Fever–≥39.0°C; Headache, Malaise, Myalgia, and Shivering–Significant, prevents daily activity.

End point type	Primary

End point timeframe:

Day 0 up to Day 7 post-any vaccination

Notes:

[35] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[36] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months	7.5 µg HA; 6-11 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	50	52	51
Units: Percentage of subjects				
number (not applicable)				
Inj. site Tenderness	33.3	24.5	46.2	17.6
Grade 3 Inj. site Tenderness	0	0	0	0
Inj. site Erythema	25	22	50	17.6
Grade 3 Inj. site Erythema	2.1	4	0	0
Inj. site Swelling	12.5	8.2	17.3	3.9
Grade 3 Inj. site Swelling	0	2	0	0
Inj. site Induration	25	24.5	36.5	17.6
Grade 3 Inj. site Induration	0	4.1	1.9	0
Inj. site Ecchymosis	6.3	14.3	13.5	9.8
Grade 3 Inj. site Ecchymosis	0	0	0	0
Fever	35.4	46	42.3	13.7
Grade 3 Fever	2.1	6	3.8	0
Vomiting	33.3	22.4	23.1	13.7
Grade 3 Vomiting	0	0	0	0
Crying abnormal	60.4	53.1	57.7	52.9
Grade 3 Crying abnormal	8.3	4.1	1.9	0
Drowsiness	43.8	28.6	51.9	33.3
Grade 3 Drowsiness	4.2	0	1.9	2
Appetite lost	47.9	42.9	48.1	49
Grade 3 Appetite lost	2.1	2	0	3.9
Irritability	66.7	57.1	69.2	76.5
Grade 3 Irritability	2.1	2	1.9	3.9

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 24-35 Months with at Least One Solicited

Reaction Listed in the EMA Note for Guidance Within 3 Days After Any and Each Vaccination with Intramuscular Inactivated, Split Virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 24-35 Months with at Least One Solicited Reaction Listed in the EMA Note for Guidance Within 3 Days After Any and Each Vaccination with Intramuscular Inactivated, Split Virion A/H1N1 Influenza Vaccine With or Without Adjuvant[37][38]

End point description:

Solicited injection site reactions: Injection site induration ≥5 cm for at least 4 consecutive days and Injection site ecchymosis. Solicited systemic reactions: Pyrexia (recorded temperature > 38°C) for at least 1 day, Malaise, and Shivering.

End point type	Primary

End point timeframe:

Day 0 up to Day 3 post-any and each vaccination

Notes:

[37] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[38] - 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: Descriptive analyses were performed based on the age group specified.

End point values	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	37	40
Units: Percentage of subjects				
number (not applicable)				
Reaction listed in the EMA recommendations	35.3	40	32.4	38.5
Reaction listed in EMA recommendations;Post-inj. 1	20.6	14.3	21.6	25.6
Reaction listed in EMA recommendations;Post-inj. 2	29.4	28.6	21.6	23.7
Inj. site Induration ≥5 cm for 4 days	0	0	0	0
Inj. site Induration ≥5 cm for 4 days; Post-inj. 1	0	0	0	0
Inj. site Induration ≥5 cm for 4 days; Post-inj. 2	0	0	0	0
Inj. site Ecchymosis	11.8	25.7	10.8	17.9
Inj. site Ecchymosis; Post-inj. 1	5.9	11.4	5.4	12.8
Inj. site Ecchymosis; Post-inj. 2	5.9	17.1	5.4	10.5
Pyrexia (temp. > 38°C) for 1 day	11.8	8.6	10.8	2.6
Pyrexia (temp. > 38°C) for 1 day; Post-inj. 1	0	2.9	2.7	2.6
Pyrexia (temp. > 38°C) for 1 day; Post-inj. 2	11.8	5.7	8.1	0
Malaise	29.4	5.7	8.1	20.5
Malaise; Post-inj. 1	17.6	0	5.6	7.7
Malaise; Post-inj. 2	17.6	5.7	8.1	13.2
Shivering	17.6	0	21.6	2.6
Shivering; Post-inj. 1	5.9	0	16.7	2.6
Shivering; Post-inj. 2	17.6	0	10.8	2.6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 (post-vaccination) up to Day 21 post-vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	1.9 µg HA + ½ AF03; 6-11 months

Reporting group description:

Subjects aged 6-11 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.

Reporting group title	3.8 µg HA + ½ AF03; 6-11 months

Reporting group description:

Subjects aged 6-11 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.

Reporting group title	3.8 µg HA + AF03; 6-11 months

Reporting group description:

Subjects aged 6-11 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.

Reporting group title	7.5 µg HA; 6-11 months

Reporting group description:

Subjects aged 6-11 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.

Reporting group title	1.9 µg HA + ½ AF03; 12-35 months

Reporting group description:

Subjects aged 12-35 months who received the half-dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (1.9 µg HA + ½ AF03 group) on Day 0 and 21.

Reporting group title	3.8 µg HA + ½ AF03; 12-35 months

Reporting group description:

Subjects aged 12-35 months who received the half-dose of the 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + ½ AF03 group) on Day 0 and 21.

Reporting group title	3.8 µg HA + AF03; 12-35 months

Reporting group description:

Subjects aged 12-35 months who received a full dose of the 3.8 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03 (3.8 µg HA + AF03 group) on Day 0 and 21.

Reporting group title	7.5 µg HA; 12-35 months

Reporting group description:

Subjects aged 12-35 months who received a half-dose of the 7.5 µg HA non-adjuvanted A/H1N1 pandemic influenza vaccine on Day 0 and 21.

Serious adverse events	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 48 (6.25%)	4 / 50 (8.00%)	3 / 52 (5.77%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Injury, poisoning and procedural complications			
Traumatic brain injury			
subjects affected / exposed	0 / 48 (0.00%)	0 / 50 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Duchenne muscular dystrophy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (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			
Febrile convulsion			
subjects affected / exposed	1 / 48 (2.08%)	0 / 50 (0.00%)	0 / 52 (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
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 48 (2.08%)	0 / 50 (0.00%)	0 / 52 (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			
Bronchitis			
subjects affected / exposed	1 / 48 (2.08%)	1 / 50 (2.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 48 (0.00%)	0 / 50 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	0 / 48 (0.00%)	1 / 50 (2.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 48 (2.08%)	1 / 50 (2.00%)	0 / 52 (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
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (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
Sepsis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 50 (2.00%)	0 / 52 (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

Serious adverse events	7.5 µg HA; 6-11 months	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 51 (5.88%)	1 / 48 (2.08%)	1 / 50 (2.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Traumatic brain injury			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 50 (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			
Duchenne muscular dystrophy			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 50 (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			
Febrile convulsion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 50 (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			
Bronchitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 50 (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 rotavirus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 50 (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
Oral herpes			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 50 (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	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 50 (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
Respiratory syncytial virus bronchitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 50 (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
Sepsis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 50 (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	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 52 (1.92%)	2 / 50 (4.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Injury, poisoning and procedural complications			
Traumatic brain injury			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Duchenne muscular dystrophy			
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (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			
Bronchitis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (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	1.9 µg HA + ½ AF03; 6-11 months	3.8 µg HA + ½ AF03; 6-11 months	3.8 µg HA + AF03; 6-11 months
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 48 (66.67%)	28 / 50 (56.00%)	36 / 52 (69.23%)
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[1]	21 / 48 (43.75%)	14 / 49 (28.57%)	27 / 52 (51.92%)
occurrences (all)	25	23	35
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[2]	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 48 (4.17%)	4 / 50 (8.00%)	1 / 52 (1.92%)
occurrences (all)	3	5	2
Injection site tenderness			
alternative assessment type: Systematic			
subjects affected / exposed[3]	16 / 48 (33.33%)	12 / 49 (24.49%)	24 / 52 (46.15%)
occurrences (all)	22	16	32

Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[4]	12 / 48 (25.00%)	11 / 50 (22.00%)	26 / 52 (50.00%)
occurrences (all)	14	14	29
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[5]	6 / 48 (12.50%)	4 / 49 (8.16%)	9 / 52 (17.31%)
occurrences (all)	7	4	9
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[6]	3 / 48 (6.25%)	7 / 49 (14.29%)	7 / 52 (13.46%)
occurrences (all)	3	8	7
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[7]	17 / 48 (35.42%)	23 / 50 (46.00%)	22 / 52 (42.31%)
occurrences (all)	19	26	26
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[9]	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 48 (8.33%)	4 / 50 (8.00%)	7 / 52 (13.46%)
occurrences (all)	5	6	10
Teething			
subjects affected / exposed	8 / 48 (16.67%)	14 / 50 (28.00%)	8 / 52 (15.38%)
occurrences (all)	12	19	8
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed[10]	16 / 48 (33.33%)	11 / 49 (22.45%)	12 / 52 (23.08%)
occurrences (all)	23	13	13

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 48 (4.17%)	2 / 50 (4.00%)	3 / 52 (5.77%)
occurrences (all)	2	2	3
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[11]	12 / 48 (25.00%)	12 / 49 (24.49%)	19 / 52 (36.54%)
occurrences (all)	14	15	20
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed[12]	29 / 48 (60.42%)	26 / 49 (53.06%)	30 / 52 (57.69%)
occurrences (all)	36	37	35
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[13]	32 / 48 (66.67%)	28 / 49 (57.14%)	36 / 52 (69.23%)
occurrences (all)	45	41	48
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[14]	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Ear infection			
subjects affected / exposed	4 / 48 (8.33%)	3 / 50 (6.00%)	1 / 52 (1.92%)
occurrences (all)	4	3	1
Gastroenteritis			
subjects affected / exposed	2 / 48 (4.17%)	3 / 50 (6.00%)	1 / 52 (1.92%)
occurrences (all)	2	3	1
Nasopharyngitis			
subjects affected / exposed	11 / 48 (22.92%)	6 / 50 (12.00%)	3 / 52 (5.77%)
occurrences (all)	13	6	3

Otitis media			
subjects affected / exposed	10 / 48 (20.83%)	5 / 50 (10.00%)	5 / 52 (9.62%)
occurrences (all)	10	6	5
Respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 50 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	9 / 48 (18.75%)	10 / 50 (20.00%)	12 / 52 (23.08%)
occurrences (all)	10	11	14
Upper respiratory tract infection			
subjects affected / exposed	7 / 48 (14.58%)	7 / 50 (14.00%)	10 / 52 (19.23%)
occurrences (all)	8	7	14
Metabolism and nutrition disorders			
Appetite lost			
alternative assessment type: Systematic			
subjects affected / exposed[15]	23 / 48 (47.92%)	21 / 49 (42.86%)	25 / 52 (48.08%)
occurrences (all)	30	28	30

Non-serious adverse events	7.5 µg HA; 6-11 months	1.9 µg HA + ½ AF03; 12-35 months	3.8 µg HA + ½ AF03; 12-35 months
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 51 (76.47%)	28 / 48 (58.33%)	28 / 50 (56.00%)
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[1]	17 / 51 (33.33%)	4 / 14 (28.57%)	4 / 15 (26.67%)
occurrences (all)	20	6	5
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[2]	0 / 51 (0.00%)	3 / 34 (8.82%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 51 (9.80%)	0 / 48 (0.00%)	0 / 50 (0.00%)
occurrences (all)	5	0	0
Injection site tenderness			
alternative assessment type: Systematic			

subjects affected / exposed[3]	9 / 51 (17.65%)	0 / 48 (0.00%)	0 / 50 (0.00%)
occurrences (all)	12	0	0
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[4]	9 / 51 (17.65%)	18 / 48 (37.50%)	16 / 50 (32.00%)
occurrences (all)	12	23	19
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[5]	2 / 51 (3.92%)	7 / 48 (14.58%)	6 / 50 (12.00%)
occurrences (all)	2	7	6
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[6]	5 / 51 (9.80%)	6 / 48 (12.50%)	14 / 50 (28.00%)
occurrences (all)	5	6	16
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[7]	7 / 51 (13.73%)	4 / 14 (28.57%)	3 / 15 (20.00%)
occurrences (all)	9	5	3
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 51 (0.00%)	10 / 34 (29.41%)	3 / 35 (8.57%)
occurrences (all)	0	12	3
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[9]	0 / 51 (0.00%)	6 / 34 (17.65%)	1 / 35 (2.86%)
occurrences (all)	0	8	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 51 (5.88%)	2 / 48 (4.17%)	3 / 50 (6.00%)
occurrences (all)	3	2	3
Teething			
subjects affected / exposed	15 / 51 (29.41%)	0 / 48 (0.00%)	0 / 50 (0.00%)
occurrences (all)	19	0	0
Vomiting			
alternative assessment type: Systematic			

subjects affected / exposed[10]	7 / 51 (13.73%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	7	1	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 51 (9.80%)	3 / 48 (6.25%)	5 / 50 (10.00%)
occurrences (all)	5	3	5
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 51 (0.00%)	3 / 48 (6.25%)	2 / 50 (4.00%)
occurrences (all)	0	3	2
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[11]	9 / 51 (17.65%)	10 / 48 (20.83%)	15 / 50 (30.00%)
occurrences (all)	10	12	18
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed[12]	27 / 51 (52.94%)	4 / 14 (28.57%)	7 / 15 (46.67%)
occurrences (all)	38	4	9
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[13]	39 / 51 (76.47%)	5 / 14 (35.71%)	9 / 15 (60.00%)
occurrences (all)	57	8	14
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[14]	0 / 51 (0.00%)	9 / 34 (26.47%)	5 / 35 (14.29%)
occurrences (all)	0	10	6
Infections and infestations			
Ear infection			
subjects affected / exposed	2 / 51 (3.92%)	0 / 48 (0.00%)	0 / 50 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	3 / 51 (5.88%)	0 / 48 (0.00%)	0 / 50 (0.00%)
occurrences (all)	3	0	0
Nasopharyngitis			

subjects affected / exposed	5 / 51 (9.80%)	3 / 48 (6.25%)	7 / 50 (14.00%)
occurrences (all)	5	3	7
Otitis media			
subjects affected / exposed	7 / 51 (13.73%)	0 / 48 (0.00%)	0 / 50 (0.00%)
occurrences (all)	7	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Rhinitis			
subjects affected / exposed	9 / 51 (17.65%)	6 / 48 (12.50%)	9 / 50 (18.00%)
occurrences (all)	10	7	12
Upper respiratory tract infection			
subjects affected / exposed	11 / 51 (21.57%)	6 / 48 (12.50%)	4 / 50 (8.00%)
occurrences (all)	11	6	4
Metabolism and nutrition disorders			
Appetite lost			
alternative assessment type: Systematic			
subjects affected / exposed[15]	25 / 51 (49.02%)	7 / 14 (50.00%)	9 / 15 (60.00%)
occurrences (all)	30	9	12

Non-serious adverse events	3.8 µg HA + AF03; 12-35 months	7.5 µg HA; 12-35 months	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 52 (55.77%)	19 / 50 (38.00%)	
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[1]	6 / 15 (40.00%)	4 / 10 (40.00%)	
occurrences (all)	9	4	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[2]	2 / 37 (5.41%)	2 / 39 (5.13%)	
occurrences (all)	2	3	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	

Injection site tenderness			
alternative assessment type: Systematic			
subjects affected / exposed[3]	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[4]	28 / 52 (53.85%)	12 / 49 (24.49%)	
occurrences (all)	36	14	
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[5]	12 / 52 (23.08%)	7 / 49 (14.29%)	
occurrences (all)	15	7	
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[6]	5 / 52 (9.62%)	8 / 49 (16.33%)	
occurrences (all)	5	10	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[7]	4 / 15 (26.67%)	2 / 10 (20.00%)	
occurrences (all)	6	2	
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[8]	4 / 37 (10.81%)	10 / 39 (25.64%)	
occurrences (all)	6	12	
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[9]	9 / 37 (24.32%)	1 / 39 (2.56%)	
occurrences (all)	11	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Teething			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	

Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed[10]	0 / 15 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 52 (7.69%)	2 / 50 (4.00%)	
occurrences (all)	4	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 52 (0.00%)	2 / 50 (4.00%)	
occurrences (all)	0	2	
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[11]	10 / 52 (19.23%)	5 / 49 (10.20%)	
occurrences (all)	13	7	
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed[12]	8 / 15 (53.33%)	5 / 10 (50.00%)	
occurrences (all)	11	5	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[13]	10 / 15 (66.67%)	6 / 10 (60.00%)	
occurrences (all)	15	8	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[14]	9 / 37 (24.32%)	5 / 39 (12.82%)	
occurrences (all)	13	7	
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			

subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	3 / 52 (5.77%)	6 / 50 (12.00%)	
occurrences (all)	3	6	
Otitis media			
subjects affected / exposed	0 / 52 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	3 / 52 (5.77%)	1 / 50 (2.00%)	
occurrences (all)	3	1	
Rhinitis			
subjects affected / exposed	5 / 52 (9.62%)	6 / 50 (12.00%)	
occurrences (all)	5	6	
Upper respiratory tract infection			
subjects affected / exposed	7 / 52 (13.46%)	3 / 50 (6.00%)	
occurrences (all)	7	3	
Metabolism and nutrition disorders			
Appetite lost			
alternative assessment type: Systematic			
subjects affected / exposed[15]	11 / 15 (73.33%)	4 / 10 (40.00%)	
occurrences (all)	16	5	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable}

days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 {or 3 as applicable} days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2009	The modalities of physical examination to be performed by investigators were changed.
01 February 2010	Documented the persistence of anti-HA antibodies in a subset of subjects who received two half-doses of either the 15 µg HA or 3.8 µg HA + AF03 vaccine (i.e. 7.5 µg HA and 1.9 µg HA + ½ AF03 doses, respectively). The subjects included in the antibody persistence evaluation were followed for persistence of the immune response 8 months after the first A/H1N1 vaccination. One more visit (V05) was planned 8 months after the first vaccination to perform blood sampling for the subjects who participated in antibody persistence evaluation.
30 June 2010	Evaluated the safety and the immune response to the seasonal trivalent seasonal influenza vaccine 2010-2011 NH formulation on the subjects previously vaccinated with two half-doses of the 3.8 µg HA + AF03 or the unadjuvanted 15 µg HA pandemic influenza vaccines. For subjects aged more than 36 months, two visits, Visit 06, planned one year after the first A/H1N1 pandemic influenza vaccine injection and Visit 07, planned 21 days after Visit 06, were added. For subjects aged less than 36 months, three visits, Visit 06, planned one year after the first A/H1N1 pandemic influenza vaccine injection, Visit 07, planned 21 to 28 days after Visit 06 and Visit 08 planned 42 to 45 days after Visit 6 were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported