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 3 to 17 Years

Summary

EudraCT number	2009-013346-83
Trial protocol	FI
Global end of trial date	02 November 2010

Results information

Result version number	v1 (current)
This version publication date	05 February 2016
First version publication date	29 January 2015

Trial information

Trial identification

Sponsor protocol code	GPF08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00956202
WHO universal trial number (UTN)	U1111-1111-4962

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	01 April 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 November 2010
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 HAI and SN testing in all subjects.
•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 antibody persistence eight months (M8) after the first vaccine administration using HAI method, in a subset of subjects who received two injections of either the 15 µg HA or 3.8 µg HA + AF03 vaccine (amendment 2)
•To describe the immune response against the A/H1N1 strain using HAI method 21 days after a vaccination with the 2010-2011 NH seasonal TIV administered approximately 13 months after the first vaccination in the subset of subjects who received two injections of either the 15 µg HA or 3.8 µg HA + AF03 vaccine for primary vaccination 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 15 µg dose of non-adjuvanted formulation was chosen based on Sanofi Pasteur experience with seasonal influenza vaccine 15 µg (Vaxigrip®). This formulation used as safety control to the adjuvanted groups.

Actual start date of recruitment	18 August 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: 303
Worldwide total number of subjects	303
EEA total number of subjects	303

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)	204
Adolescents (12-17 years)	99
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 18 August 2009 to 25 August 2009 in 15 clinical centers in Finland.

Pre-assignment

Screening details:

A total of 303 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	3.8 µg HA+AF03; 9-17 years

Arm description:

Subjects aged 9-17 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (3.8 µg HA + AF03) 21 days apart.

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 to be injected into the deltoid area, two doses 21 days apart.

Arm title	7.5 µg HA+AF03; 9-17 years

Arm description:

Subjects aged 9-17 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (7.5 µg HA + AF03) 21 days apart.

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 to be injected into the deltoid area, two doses 21 days apart.

Arm title	15 µg HA; 9-17 years

Arm description:

Subjects aged 9-17 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.

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:

0.5 mL dose, intramuscular to be injected into the deltoid area, two doses 21 days apart.

Arm title	3.8 µg HA+AF03; 3-8 years

Arm description:

Subjects aged 3-8 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (3.8 µg HA + AF03) 21 days apart.

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 to be injected into the deltoid area, two doses 21 days apart.

Arm title	7.5 µg HA+AF03; 3-8 years

Arm description:

Subjects aged 3-8 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (7.5 µg HA + AF03) 21 days apart.

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 to be injected into the deltoid area, two doses 21 days apart.

Arm title	15 µg HA; 3-8 years

Arm description:

Subjects aged 3-8 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.

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:

0.5 mL dose, intramuscular to be injected into the deltoid area, two doses 21 days apart.

Number of subjects in period 1	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years
Started	49	50	52
Completed	49	49	52
Not completed	0	1	0
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years
Started	50	50	52
Completed	50	49	50
Not completed	0	1	2
Consent withdrawn by subject	-	-	2
Adverse event, non-fatal	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	3.8 µg HA+AF03; 9-17 years
Reporting group description:	
Subjects aged 9-17 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (3.8 µg HA + AF03) 21 days apart.	
Reporting group title	7.5 µg HA+AF03; 9-17 years
Reporting group description:	
Subjects aged 9-17 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (7.5 µg HA + AF03) 21 days apart.	
Reporting group title	15 µg HA; 9-17 years
Reporting group description:	
Subjects aged 9-17 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.	
Reporting group title	3.8 µg HA+AF03; 3-8 years
Reporting group description:	
Subjects aged 3-8 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (3.8 µg HA + AF03) 21 days apart.	
Reporting group title	7.5 µg HA+AF03; 3-8 years
Reporting group description:	
Subjects aged 3-8 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (7.5 µg HA + AF03) 21 days apart.	
Reporting group title	15 µg HA; 3-8 years
Reporting group description:	
Subjects aged 3-8 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.	

Reporting group values	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years
Number of subjects	49	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)	0	0	0
Children (2-11 years)	16	21	15
Adolescents (12-17 years)	33	29	37
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	12.7	12.9	12.5
standard deviation	± 2.4	± 2.7	± 2.3
Gender categorical Units: Subjects			
Female	26	20	27
Male	23	30	25

Influenza vaccination 2008/2009 Units: Subjects			
Yes	12	9	10
No	37	40	42
Unknown	0	1	0
Influenza vaccination 2007/2008 Units: Subjects			
Yes	4	8	5
No	45	41	46
Unknown	0	1	1
Influenza vaccination 2006/2007 Units: Subjects			
Yes	0	2	2
No	49	46	50
Unknown	0	2	0
Influenza vaccination 2005/2006 Units: Subjects			
Yes	0	1	1
No	49	47	51
Unknown	0	2	0
Not applicable	0	0	0
Influenza vaccination 2004/2005 Units: Subjects			
Yes	1	2	1
No	48	46	51
Unknown	0	2	0
Not applicable	0	0	0
Subjects in contact with a confirmed and/or probable case of H1N1 within 8 months of enrollment Units: Subjects			
No	49	46	50
Unknown	0	4	2

Reporting group values	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years
Number of subjects	50	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)	0	0	0
Children (2-11 years)	50	50	52
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: years			
arithmetic mean	5.6	5.6	6.1

standard deviation	± 1.8	± 1.9	± 1.8

Gender categorical Units: Subjects			
Female	31	22	30
Male	19	28	22
Influenza vaccination 2008/2009 Units: Subjects			
Yes	16	21	19
No	33	29	32
Unknown	1	0	1
Influenza vaccination 2007/2008 Units: Subjects			
Yes	11	12	12
No	38	38	39
Unknown	1	0	1
Influenza vaccination 2006/2007 Units: Subjects			
Yes	3	2	0
No	46	48	52
Unknown	1	0	0
Influenza vaccination 2005/2006 Units: Subjects			
Yes	1	1	0
No	45	41	48
Unknown	1	0	0
Not applicable	3	8	4
Influenza vaccination 2004/2005 Units: Subjects			
Yes	0	0	0
No	34	30	38
Unknown	1	0	0
Not applicable	15	20	14
Subjects in contact with a confirmed and/or probable case of H1N1 within 8 months of enrollment Units: Subjects			
No	49	49	51
Unknown	1	1	1

Reporting group values	Total		
Number of subjects	303		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	204		

Adolescents (12-17 years)	99		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	156		
Male	147		
Influenza vaccination 2008/2009 Units: Subjects			
Yes	87		
No	213		
Unknown	3		
Influenza vaccination 2007/2008 Units: Subjects			
Yes	52		
No	247		
Unknown	4		
Influenza vaccination 2006/2007 Units: Subjects			
Yes	9		
No	291		
Unknown	3		
Influenza vaccination 2005/2006 Units: Subjects			
Yes	4		
No	281		
Unknown	3		
Not applicable	15		
Influenza vaccination 2004/2005 Units: Subjects			
Yes	4		
No	247		
Unknown	3		
Not applicable	49		
Subjects in contact with a confirmed and/or probable case of H1N1 within 8 months of enrollment Units: Subjects			
No	294		
Unknown	9		

End points

End points reporting groups

Reporting group title	3.8 µg HA+AF03; 9-17 years
Reporting group description:	
Subjects aged 9-17 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (3.8 µg HA + AF03) 21 days apart.	
Reporting group title	7.5 µg HA+AF03; 9-17 years
Reporting group description:	
Subjects aged 9-17 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (7.5 µg HA + AF03) 21 days apart.	
Reporting group title	15 µg HA; 9-17 years
Reporting group description:	
Subjects aged 9-17 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.	
Reporting group title	3.8 µg HA+AF03; 3-8 years
Reporting group description:	
Subjects aged 3-8 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (3.8 µg HA + AF03) 21 days apart.	
Reporting group title	7.5 µg HA+AF03; 3-8 years
Reporting group description:	
Subjects aged 3-8 years who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (7.5 µg HA + AF03) 21 days apart.	
Reporting group title	15 µg HA; 3-8 years
Reporting group description:	
Subjects aged 3-8 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.	

Primary: Geometric Mean Titers (GMTs) of Antibody Assayed by HAI Method Against A/California (H1N1) Strain in Subjects Age 9 to 17 Years Old Following 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 HAI Method Against A/California (H1N1) Strain in Subjects Age 9 to 17 Years Old Following Vaccination with 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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	6.82 (5.45 to 8.54)	8.38 (6.62 to 10.6)	6.66 (5.24 to 8.46)	
Day 21	1208 (915 to 1595)	1544 (1158 to 2059)	830 (533 to 1292)	
Day 42	3595 (3069 to 4210)	4476 (3957 to 5064)	1584 (1208 to 2077)	

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 3 to 8 Years Old Following 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 HAI Method Against A/California (H1N1) Strain in Subjects Age 3 to 8 Years Old Following Vaccination with 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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	5.07 (4.97 to 5.17)	5.07 (4.93 to 5.21)	5 (5 to 5)	
Day 21	631 (504 to 791)	772 (594 to 1004)	175 (120 to 256)	
Day 42	4476 (3791 to 5285)	4729 (4132 to 5412)	816 (596 to 1117)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9 to 17 Years Old with Antibody titers ≥ 10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9 to 17 Years Old with Antibody titers ≥ 10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with 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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 0	22.9	30.6	11.5	
Day 21	100	100	100	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3 to 8 Years Old with Antibody titers ≥ 10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 3 to 8 Years Old with Antibody

	titers ≥ 10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with 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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	2	0	
Day 21	100	100	98	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9 to 17 Years Old with Antibody titers ≥ 40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9 to 17 Years Old with Antibody titers ≥ 40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[9][10]

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:

[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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 0	4.2	10.2	7.7	
Day 21	100	100	98.1	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3 to 8 Years Old with Antibody titers ≥ 40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 3 to 8 Years Old with Antibody titers ≥ 40 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[11][12]

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:

[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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	0	0	
Day 21	100	100	94	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9-17 Years Achieving Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9-17 Years Achieving Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[13][14]

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). Significant increase was defined as 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:

[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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 21	100	100	98.1	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3-8 Years Achieving Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine

With or Without Adjuvant

End point title	Percentage of Subjects Age 3-8 Years Achieving Seroconversion or significant increase in Antibody Assayed by HAI Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[15][16]

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). Significant increase was defined as 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:

[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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 21	100	100	94	
Day 42	100	100	100	

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 9-17 Years Old After Inactivated, Split Virion Swine-origin 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 9-17 Years Old After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[17][18]

End point description:

Immunogenicity was evaluated using the seroneutralization (SN) 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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	8.12 (5.9 to 11.2)	12.8 (8.68 to 19)	8.14 (5.77 to 11.5)	
Day 21	3661 (2763 to 4850)	4492 (3534 to 5708)	2618 (1680 to 4079)	
Day 42	9172 (8500 to 9897)	10109 (9910 to 10312)	5058 (3965 to 6453)	

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 3-8 Years After Inactivated, Split Virion Swine-origin 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 3-8 Years After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[19][20]

End point description:

Immunogenicity was evaluated using the seroneutralization (SN) 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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	5.07 (4.93 to 5.21)	5.12 (4.88 to 5.36)	5.35 (4.82 to 5.94)	
Day 21	2094 (1657 to 2646)	2791 (2113 to 3686)	660 (427 to 1019)	
Day 42	9932 (9551 to 10328)	9791 (9295 to 10314)	2583 (1937 to 3443)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9-17 Years with Neutralizing Antibody titers ≥ 40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9-17 Years with Neutralizing Antibody titers ≥ 40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[21][22]

End point description:

Immunogenicity was evaluated using the seroneutralization (SN) method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and 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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 0	8.2	26	9.6	
Day 21	100	100	100	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3-8 Years with Neutralizing Antibody titers ≥ 40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 3-8 Years with Neutralizing Antibody titers ≥ 40 (1/dil) Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[23][24]

End point description:

Immunogenicity was evaluated using the seroneutralization (SN) method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and 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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	0	1.9	
Day 21	100	100	94	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9-17 Years with 2- and 4-fold Increase in Neutralizing Antibody titers Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9-17 Years with 2- and 4-fold Increase in Neutralizing Antibody titers Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion A/H1N1 Influenza Vaccine With or Without Adjuvant[25][26]

End point description:

Immunogenicity was evaluated using the seroneutralization (SN) method.

End point type	Primary

End point timeframe:

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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
2-fold increase from Day 0; Day 21	100	100	100	
2-fold increase from Day 0; Day 42	100	100	100	
4-fold increase from Day 0; Day 21	100	100	100	
4-fold increase from Day 0; Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3-8 Years with 2- and 4-fold Increase in Neutralizing Antibody titers Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 3-8 Years with 2- and 4-fold Increase in Neutralizing Antibody titers Assayed by Seroneutralization Method Against A/California (H1N1) Strain After Inactivated, Split Virion A/H1N1 Influenza Vaccine With or Without Adjuvant[27][28]

End point description:

Immunogenicity was evaluated using the seroneutralization (SN) method.

End point type	Primary

End point timeframe:

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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Percentage of subjects				
number (not applicable)				
2-fold increase from Day 0; Day 21	100	100	98	
2-fold increase from Day 0; Day 42	100	100	100	
4-fold increase from Day 0; Day 21	100	100	96	
4-fold increase from Day 0; Day 42	100	100	100	

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 9 to 17 Years 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 9 to 17 Years Old Before and After Vaccination with 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.

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 study groups and the study vaccine administered for this outcome.
[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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Titers (mm2)				
geometric mean (confidence interval 95%)				
Day 0	8.37 (6.27 to 11.2)	12.7 (9.54 to 16.8)	12.2 (9.24 to 16.2)	

Day 21	95 (87.3 to 103)	98.3 (90.2 to 107)	94.5 (84.7 to 105)	
Day 42	117 (113 to 121)	118 (114 to 123)	104 (96.5 to 112)	

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 3 to 8 Years 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 3 to 8 Years Old Before and After Vaccination with 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.

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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Titers (mm2)				
geometric mean (confidence interval 95%)				
Day 0	9.29 (7.43 to 11.6)	11.9 (9.15 to 15.4)	8.41 (6.57 to 10.8)	
Day 21	87.1 (81.3 to 93.3)	94.3 (88 to 101)	64.7 (54.3 to 77.2)	
Day 42	116 (111 to 121)	118 (114 to 123)	80.9 (73.1 to 89.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9-17 Years Achieving Seroconversion or significant increase in Antibody Assayed by SRH Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9-17 Years Achieving Seroconversion or significant increase in Antibody Assayed by SRH Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[33][34]

End point description:

Immunogenicity was evaluated using Single radial hemolysis (SRH) testing. Seroconversion was defined as subjects with a pre-vaccination titer ≤4 mm² on Day 0: post-injection titer ≥25 mm² on Day 21 or Day 42 or significant increase for subjects with a pre-vaccination titer >4 mm²: ≥1.5-fold increase of post-injection titer on Day 21 or Day 42.

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 21/Day 0	95.9	97.9	96.2	
Day 42/Day 0	98	97.9	98.1	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3-8 Years Achieving Seroconversion or significant increase in Antibody Assayed by SRH Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine Wi

End point title	Percentage of Subjects Age 3-8 Years Achieving Seroconversion or significant increase in Antibody Assayed by SRH Method Against A/California (H1N1) Strain After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine Wi[35][36]

End point description:

Immunogenicity was evaluated using Single radial hemolysis (SRH) testing. Seroconversion was defined as subjects with a pre-vaccination titer ≤4 mm² on Day 0: post-injection titer ≥25 mm² on Day 21 or Day 42 or significant increase for subjects with a pre-vaccination titer >4 mm²: ≥1.5-fold increase of post-injection titer on Day 21 or Day 42.

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	52	
Units: Percentage of subjects				
number (not applicable)				
Day 21/Day 0	100	100	87.8	
Day 42/Day 0	100	100	95.9	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9 to 17 Years Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9 to 17 Years Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[37][38]

End point description:

Solicited injection site: Pain, Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 Solicited Injection site reactions (3-11 years): Pain – Incapacitating, preventing the performance of usual activities; Erythema, Swelling, Induration, and Ecchymosis - ≥5 cm. Grade 3 Solicited Injection site reactions (≥12 years): Significant, prevents daily activity; Erythema, Swelling, Induration, and Ecchymosis - >10 cm. Grade 3 Solicited systemic reactions: Fever - ≥39°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:

[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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	89.8	90	76.9	
Grade 3 Injection site Pain	2	0	0	
Injection site Erythema	38.8	26	11.5	
Grade 3 Injection site Erythema	8.2	4	0	
Injection site Swelling	20.4	14	5.8	
Grade 3 Injection site Swelling	2	2	0	
Injection site Induration	18.4	16	5.8	
Grade 3 Injection site Induration	2	2	0	
Injection site Ecchymosis	6.1	12	3.8	
Grade 3 Injection site Ecchymosis	0	0	0	
Fever	12.2	16	5.8	
Grade 3 Fever	0	4	3.8	
Headache	69.4	66	50	
Grade 3 Headache	4.1	8	3.8	
Malaise	57.1	50	36.5	
Grade 3 Malaise	10.2	14	3.8	
Myalgia	49	44	32.7	
Grade 3 Myalgia	4.1	12	1.9	
Shivering	46.9	40	21.2	
Grade 3 Shivering	2	10	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3 to 8 Years Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 3 to 8 Years Old Reporting Solicited Injection-site or Systemic Reactions After Any Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[39][40]

End point description:

Solicited injection site: Pain, Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 Solicited Injection site reactions (3-11 years): Pain – Incapacitating, preventing the performance of usual activities; Erythema, Swelling, Induration, and Ecchymosis - ≥5 cm. Grade 3 Solicited systemic reactions: Fever - ≥39°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:

[39] - 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.

[40] - 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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	51	
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	88	74.5	60.8	
Grade 3 Injection site Pain	2	2	0	
Injection site Erythema	50	62.7	23.5	
Grade 3 Injection site Erythema	18	19.6	3.9	
Injection site Swelling	28	43.1	7.8	
Grade 3 Injection site Swelling	8	7.8	0	
Injection site Induration	22	27.5	13.7	
Grade 3 Injection site Induration	2	0	0	
Injection site Ecchymosis	26	17.6	13.7	
Grade 3 Injection site Ecchymosis	0	0	0	
Fever	24	23.5	5.9	
Grade 3 Fever	2	3.9	0	
Headache	42	43.1	25.5	
Grade 3 Headache	2	7.8	2	
Malaise	44	37.3	25.5	
Grade 3 Malaise	2	5.9	2	
Myalgia	44	33.3	15.7	
Grade 3 Myalgia	2	2	3.9	
Shivering	28	35.3	15.7	
Grade 3 Shivering	0	2	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 9-17 Years with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Any and Each Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 9-17 Years with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Any and Each Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[41][42]

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:

[41] - 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.
[42] - 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	3.8 µg HA+AF03; 9-17 years	7.5 µg HA+AF03; 9-17 years	15 µg HA; 9-17 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	50	52	
Units: Percentage of subjects				
number (not applicable)				
Reaction listed in the EMA recommendation	67.3	56	42.3	
Reaction listed in EMA recommendation; Post-inj. 1	49	42	34.6	
Reaction listed in EMA recommendation; Post-inj. 2	32.7	32.7	11.5	
Inj. site Induration ≥5 cm for 4 days	0	0	0	
Inj. site Induration ≥5 cm for 4 days; Post-inj. 1	0	0	0	
Inj. site Induration ≥5 cm for 4 days; Post-inj. 2	0	0	0	
Inj. site Ecchymosis	10.2	14	13.5	
Inj. site Ecchymosis; Post-inj. 1	10.2	14	9.6	
Inj. site Ecchymosis; Post-inj. 2	0	2	3.8	
Pyrexia (temp. >38°C) for 1 day	8.2	12	3.8	
Pyrexia (temp. >38°C) for 1 day; Post-inj. 1	4.1	4	1.9	
Pyrexia (temp. >38°C) for 1 day; Post-inj. 2	4.1	10.2	1.9	
Malaise	51	44	30.8	
Malaise; Post-inj. 1	32.7	26	25	
Malaise; Post-inj. 2	30.6	28.6	9.6	
Shivering	44.9	36	13.5	
Shivering; Post-inj. 1	24.5	22	7.7	
Shivering; Post-inj. 2	24.5	18.4	5.8	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 3-8 Years with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Any and Each Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 3-8 Years with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Any and Each Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without

	Adjuvant[43][44]

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:

[43] - 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.
[44] - 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	3.8 µg HA+AF03; 3-8 years	7.5 µg HA+AF03; 3-8 years	15 µg HA; 3-8 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	51	
Units: Percentage of subjects				
number (not applicable)				
Reaction listed in the EMA recommendation	64	56.9	41.2	
Reaction listed in EMA recommendation; Post-inj. 1	36	45.1	29.4	
Reaction listed in EMA recommendation; Post-inj. 2	48	32	20.4	
Inj. site Induration ≥5 cm for 4 days	0	0	0	
Inj. site Induration ≥5 cm for 4 days; Post-inj. 1	0	0	0	
Inj. site Induration ≥5 cm for 4 days; Post-inj. 2	0	0	0	
Inj. site Ecchymosis	24	17.6	11.8	
Inj. site Ecchymosis; Post-inj. 1	14	13.7	5.9	
Inj. site Ecchymosis; Post-inj. 2	12	4	6.1	
Pyrexia (temp. > 38°C) for 1 day	14	21.6	0	
Pyrexia (temp. > 38°C) for 1 day; Post-inj. 1	2	11.8	0	
Pyrexia (temp. > 38°C) for 1 day; Post-inj. 2	12	12	0	
Malaise	42	33.3	21.6	
Malaise; Post-inj. 1	20	25.5	17.6	
Malaise; Post-inj. 2	34	20	10.2	
Shivering	28	35.3	13.7	
Shivering; Post-inj. 1	16	23.5	9.8	
Shivering; Post-inj. 2	16	16	4.1	

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	3.8 µg HA+AF03 (All groups)
Reporting group description:	
Subjects who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (3.8 µg HA + AF03) 21 days apart.	
Reporting group title	7.5 µg HA+AF03 (All groups)
Reporting group description:	
Subjects who received two doses of adjuvanted A/H1N1 pandemic influenza vaccine (7.5 µg HA + AF03) 21 days apart.	
Reporting group title	15 µg HA (All groups)
Reporting group description:	
Subjects who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.	

Serious adverse events	3.8 µg HA+AF03 (All groups)	7.5 µg HA+AF03 (All groups)	15 µg HA (All groups)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 99 (1.01%)	2 / 101 (1.98%)	4 / 103 (3.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 99 (0.00%)	0 / 101 (0.00%)	1 / 103 (0.97%)
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 upper			
subjects affected / exposed	0 / 99 (0.00%)	0 / 101 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 99 (0.00%)	0 / 101 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis reactive			
subjects affected / exposed	0 / 99 (0.00%)	0 / 101 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 101 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 101 (0.00%)	0 / 103 (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
Pneumonia			
subjects affected / exposed	0 / 99 (0.00%)	1 / 101 (0.99%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 99 (0.00%)	1 / 101 (0.99%)	0 / 103 (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

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

Non-serious adverse events	3.8 µg HA+AF03 (All groups)	7.5 µg HA+AF03 (All groups)	15 µg HA (All groups)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 99 (88.89%)	83 / 101 (82.18%)	71 / 103 (68.93%)
Nervous system disorders			

Headache			
alternative assessment type: Systematic			
subjects affected / exposed	55 / 99 (55.56%)	55 / 101 (54.46%)	39 / 103 (37.86%)
occurrences (all)	75	74	53
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	88 / 99 (88.89%)	83 / 101 (82.18%)	71 / 103 (68.93%)
occurrences (all)	149	140	106
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	44 / 99 (44.44%)	45 / 101 (44.55%)	18 / 103 (17.48%)
occurrences (all)	59	63	23
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 99 (24.24%)	29 / 101 (28.71%)	7 / 103 (6.80%)
occurrences (all)	31	36	9
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 99 (16.16%)	15 / 101 (14.85%)	9 / 103 (8.74%)
occurrences (all)	18	16	10
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 99 (18.18%)	20 / 101 (19.80%)	6 / 103 (5.83%)
occurrences (all)	18	22	6
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	50 / 99 (50.51%)	44 / 101 (43.56%)	32 / 103 (31.07%)
occurrences (all)	62	56	40
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed	37 / 99 (37.37%)	38 / 101 (37.62%)	19 / 103 (18.45%)
occurrences (all)	43	42	21
Axillary pain			

subjects affected / exposed	0 / 99 (0.00%)	6 / 101 (5.94%)	1 / 103 (0.97%)
occurrences (all)	0	6	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 99 (2.02%)	2 / 101 (1.98%)	6 / 103 (5.83%)
occurrences (all)	3	2	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 99 (7.07%)	12 / 101 (11.88%)	7 / 103 (6.80%)
occurrences (all)	7	13	7
Oropharyngeal pain			
subjects affected / exposed	8 / 99 (8.08%)	10 / 101 (9.90%)	10 / 103 (9.71%)
occurrences (all)	8	11	11
Skin and subcutaneous tissue disorders			
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	20 / 99 (20.20%)	22 / 101 (21.78%)	10 / 103 (9.71%)
occurrences (all)	25	31	11
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	46 / 99 (46.46%)	39 / 101 (38.61%)	25 / 103 (24.27%)
occurrences (all)	62	47	33
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 99 (4.04%)	5 / 101 (4.95%)	12 / 103 (11.65%)
occurrences (all)	4	5	14
Respiratory tract infection			
subjects affected / exposed	5 / 99 (5.05%)	6 / 101 (5.94%)	6 / 103 (5.83%)
occurrences (all)	5	7	6
Rhinitis			
subjects affected / exposed	10 / 99 (10.10%)	17 / 101 (16.83%)	19 / 103 (18.45%)
occurrences (all)	10	21	19
Upper respiratory tract infection			
subjects affected / exposed	11 / 99 (11.11%)	11 / 101 (10.89%)	16 / 103 (15.53%)
occurrences (all)	13	12	18

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 August 2009	Involved changes in the ICFs of parents/guardians and subjects aged 12 to 17 years, as well as in the Assent Form, updated the population of subjects in which pregnancy tests were to be performed, i.e. to all subjects of childbearing age, and modified the modalities of physical examinations.
01 February 2010	Included modifications in order to assess antibody persistence 8 months after the first vaccine injection, by adding an additional visit (Visit 5) with an additional blood sampling.
23 June 2010	Included evaluation of the safety and immune response to the trivalent seasonal influenza vaccine 2010-2011 NH formulation on the study subjects previously vaccinated with the 3.8 µg HA + AF03 or the unadjuvanted 15 µg HA pandemic influenza vaccines. Two visits, Visit 6, planned one year after the first pandemic influenza vaccine injection and Visit 7, planned 21 days after Visit 6 were added to the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported