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 Adult and Elderly subjects

Summary

EudraCT number	2009-013344-37
Trial protocol	FR
Global end of trial date	08 October 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	GPF07

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00954798
WHO universal trial number (UTN)	U1111-1111-4918

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 (0)4 37 37 58 50, stephanie.pepin@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)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	24 January 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 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 hemagglutination inhibition (HAI) and seroneutralization (SN) method in all adult and elderly 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 adult and elderly subjects.

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:

Not applicable

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	France: 450
Worldwide total number of subjects	450
EEA total number of subjects	450

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	339
From 65 to 84 years	109
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled 18 August 2009 to 22 August 2009 in 12 clinical centers in France.

Pre-assignment

Screening details:

A total of 450 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	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	3.8 µg HA+AF03; 18-60 years

Arm description:

Subjects aged 18-60 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	448
Other name	
Pharmaceutical forms	Emulsion and suspension for 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; 18-60 years

Arm description:

Subjects aged 18-60 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	448
Other name	
Pharmaceutical forms	Emulsion and suspension for 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; 18-60 years

Arm description:

Subjects aged 18-60 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; >60 years

Arm description:

Subjects aged >60 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	448
Other name	
Pharmaceutical forms	Emulsion and suspension for 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; >60 years

Arm description:

Subjects aged >60 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	448
Other name	
Pharmaceutical forms	Emulsion and suspension for 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; >60 years

Arm description:

Subjects aged >60 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; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years
Started	99	100	101
Completed	98	99	101
Not completed	1	1	0
Adverse event, serious fatal	1	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years
Started	54	51	45
Completed	54	50	44
Not completed	0	1	1
Adverse event, serious fatal	-	1	1
Protocol deviation	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	3.8 µg HA+AF03; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; >60 years
Reporting group description:	
Subjects aged >60 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; >60 years
Reporting group description:	
Subjects aged >60 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; >60 years
Reporting group description:	
Subjects aged >60 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; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years
Number of subjects	99	100	101
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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	99	100	101
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	42.1	43	44.3
standard deviation	± 12.5	± 11.4	± 12.3
Gender categorical Units: Subjects			
Female	51	57	54
Male	48	43	47

Influenza vaccination 2008/2009 Units: Subjects			
Yes	19	22	24
No	80	78	77
Influenza vaccination 2007/2008 Units: Subjects			
Yes	22	20	22
No	76	80	79
Unknown	1	0	0
Influenza vaccination 2006/2007 Units: Subjects			
Yes	25	22	27
No	72	78	73
Unknown	2	0	1
Influenza vaccination 2005/2006 Units: Subjects			
Yes	18	9	16
No	78	89	83
Unknown	3	2	2
Influenza vaccination 2004/2005 Units: Subjects			
Yes	18	11	17
No	77	87	82
Unknown	4	2	2

Reporting group values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years
Number of subjects	54	51	45
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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	14	17	11
From 65-84 years	39	34	33
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	71.5	69.8	71
standard deviation	± 7.2	± 6.4	± 6.6
Gender categorical Units: Subjects			
Female	36	28	24
Male	18	23	21
Influenza vaccination 2008/2009 Units: Subjects			
Yes	46	47	40

No	8	4	5
Influenza vaccination 2007/2008 Units: Subjects			
Yes	47	45	40
No	6	5	5
Unknown	1	1	0
Influenza vaccination 2006/2007 Units: Subjects			
Yes	47	44	40
No	7	7	5
Unknown	0	0	0
Influenza vaccination 2005/2006 Units: Subjects			
Yes	35	30	30
No	17	19	14
Unknown	2	2	1
Influenza vaccination 2004/2005 Units: Subjects			
Yes	35	28	29
No	17	19	15
Unknown	2	4	1

Reporting group values	Total		
Number of subjects	450		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	342		
From 65-84 years	106		
85 years and over	2		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	250		
Male	200		
Influenza vaccination 2008/2009 Units: Subjects			
Yes	198		
No	252		
Influenza vaccination 2007/2008 Units: Subjects			
Yes	196		

No	251		
Unknown	3		
Influenza vaccination 2006/2007 Units: Subjects			
Yes	205		
No	242		
Unknown	3		
Influenza vaccination 2005/2006 Units: Subjects			
Yes	138		
No	300		
Unknown	12		
Influenza vaccination 2004/2005 Units: Subjects			
Yes	138		
No	297		
Unknown	15		

End points

End points reporting groups

Reporting group title	3.8 µg HA+AF03; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; >60 years
Reporting group description:	
Subjects aged >60 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; >60 years
Reporting group description:	
Subjects aged >60 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; >60 years
Reporting group description:	
Subjects aged >60 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.	

Primary: Percentage of Subjects Age 18-60 Years with Antibody titers ≥10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Before and After Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age 18-60 Years with Antibody titers ≥10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Before and After 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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
Day 0	44.4	45	40.6	
Day 21	100	100	98	
Day 42	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age Over 60 Years with Antibody titers ≥10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Before and After Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Subjects Age Over 60 Years with Antibody titers ≥10 (1/dil) Assayed by HAI Method Against A/California (H1N1) Strain Before and After 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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
Day 0	59.3	49	45.5	
Day 21	98.1	97.9	97.7	
Day 42	100	100	100	

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 18-60 Years 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 HAI Method Against A/California (H1N1) Strain in Subjects Age 18-60 Years Before and After 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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	10.9 (8.5 to 13.9)	9.56 (7.98 to 11.4)	10.5 (8.49 to 13)	
Day 21	826 (624 to 1094)	787 (625 to 990)	514 (362 to 732)	
Day 42	1205 (979 to 1482)	1198 (997 to 1438)	616 (464 to 819)	

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 Over 60 Years 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 HAI Method Against A/California (H1N1) Strain in Subjects Over 60 Years Before and After 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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	11.4 (8.88 to 14.6)	10.7 (8.27 to 13.7)	9.84 (7.69 to 12.6)	
Day 21	184 (111 to 306)	271 (179 to 411)	182 (111 to 300)	
Day 42	298 (201 to 442)	414 (295 to 580)	277 (184 to 416)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Adult Subjects Age 18 to 60 Years Old with Seroprotection Against A/California (H1N1) Strain Before and Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Adult Subjects Age 18 to 60 Years Old with Seroprotection Against A/California (H1N1) Strain Before and 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. Seroprotection was defined as antibody titers ≥40 (1/[dil]).

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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
Day 0	14.1	10	14.9	
Day 21	97	99	93	
Day 42	100	100	98	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Elderly Subjects Age Over 60 Years Old with Seroprotection Against A/California (H1N1) Strain Before and Following Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Elderly Subjects Age Over 60 Years Old with Seroprotection Against A/California (H1N1) Strain Before and 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. Seroprotection was defined as antibody titers ≥40 (1/[dil]).

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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
Day 0	14.8	10.2	9.1	
Day 21	83.3	89.6	83.7	
Day 42	96.3	96	95.3	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 18-60 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 18-60 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 for subjects with a pre-vaccination titer <10 (1/dil) on D0, post-vaccination titer ≥40 (1/dil) or significant increase for subjects with a pre-vaccination titer ≥10 (1/dil), ≥4-fold increase of the titer (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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
Day 21	93.9	98	92	
Day 42	99	100	96	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Over 60 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 Over 60 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 for subjects with a pre-vaccination titer <10 (1/dil) on D0, post-vaccination titer ≥40 (1/dil) or significant increase for subjects with a pre-vaccination titer ≥10 (1/dil), ≥4-fold increase of the titer (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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
Day 21	74.1	85.4	81.4	
Day 42	90.7	93.8	90.7	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Age 18-60 Years Before and After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Age 18-60 Years Before and 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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	21.6 (15.6 to 29.9)	16.7 (12.7 to 22)	16.4 (12.1 to 22.2)	
Day 21	2972 (2273 to 3885)	2580 (1975 to 3371)	1500 (1050 to 2143)	
Day 42	4316 (3522 to 5290)	4203 (3395 to 5203)	1976 (1466 to 2664)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Over 60 Years Before and After Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Geometric Mean Titers of Neutralizing Antibody Assayed by Seroneutralization Method Against A/California (H1N1) Strain in Subjects Over 60 Years Before and 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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	21.6 (14.8 to 31.5)	22.7 (15.5 to 33.3)	17.9 (11.7 to 27.5)	
Day 21	536 (314 to 914)	788 (498 to 1246)	576 (343 to 968)	

Day 42	884 (567 to 1377)	1315 (912 to 1896)	822 (523 to 1291)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 18-60 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 18-60 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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
Day 0	29.3	23	29	
Day 21	99	99	97	
Day 42	100	99	98	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age Over 60 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 Over 60 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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
Day 0	33.3	31.4	28.9	
Day 21	94.4	94.1	93.2	
Day 42	98.1	100	97.7	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 18-60 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 18-60 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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
2-fold increase; Day 21	98	99	98	
2-fold increase; Day 42	99	100	99	
4-fold increase; Day 21	94.9	98	96	
4-fold increase; Day 42	95.9	99	97	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Over 60 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 Over 60 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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
2-fold increase; Day 21	94.4	94.1	93.2	
2-fold increase; Day 42	94.4	98	97.7	

4-fold increase; Day 21	85.2	86.3	88.6	
4-fold increase; Day 42	88.9	96	86.4	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Age 18-60 Years Old 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 18-60 Years Old 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[29][30]

End point description:

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

[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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
Day 21	92.9	91.9	87.1	
Day 42	98	98	95	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Over 60 Years Old 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 Over 60 Years Old 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[31][32]

End point description:

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

[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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
Day 21	64.8	74.5	72.7	
Day 42	87	84	90.9	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Adult Subjects Age 18 to 60 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 Adult Subjects Age 18 to 60 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[33][34]

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: Pain – 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:

[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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
Inj. site Pain	69.7	59	24.8	
Inj. site Pain; Post-inj. 1	63.6	55	12.9	
Inj. site Pain; Post-inj. 2	44.4	38.4	18.8	
Grade 3 Inj. site Pain	4	2	0	
Grade 3 Inj. site Pain; Post-inj. 1	2	2	0	
Grade 3 Inj. site Pain; Post-inj. 2	2	0	0	
Inj. site Erythema	7.1	10	2	
Inj. site Erythema; Post-inj. 1	5.1	10	1	
Inj. site Erythema; Post-inj. 2	3	3	1	
Grade 3 Inj. site Erythema	0	1	0	
Grade 3 Inj. site Erythema; Post-inj. 1	0	0	0	
Grade 3 Inj. site Erythema; Post-inj. 2	0	1	0	
Inj. site Swelling	6.1	5	3	
Inj. site Swelling; Post-inj. 1	2	3	2	
Inj. site Swelling; Post-inj. 2	5.1	2	2	
Grade 3 Inj. site Swelling	0	0	0	
Grade 3 Inj. site Swelling; Post-inj. 1	0	0	0	
Grade 3 Inj. site Swelling; Post-inj. 2	0	0	0	
Inj. site Induration	7.1	9	1	
Inj. site Induration; Post-inj. 1	6.1	6	0	
Inj. site Induration; Post-inj. 2	4	4	1	
Grade 3 Inj. site Induration	0	0	0	
Grade 3 Inj. site Induration; Post-inj. 1	0	0	0	
Grade 3 Inj. site Induration; Post-inj. 2	0	0	0	
Inj. site Ecchymosis	2	0	0	
Inj. site Ecchymosis; Post-inj. 1	1	0	0	
Inj. site Ecchymosis; Post-inj. 2	1	0	0	
Grade 3 Inj. site Ecchymosis	0	0	0	
Grade 3 Inj. site Ecchymosis; Post-inj. 1	0	0	0	
Grade 3 Inj. site Ecchymosis; Post-inj. 2	0	0	0	
Solicited inj. site reaction	70.7	62	27.7	
Solicited inj. site reaction; Post-inj. 1	64.6	58	14.9	
Solicited inj. site reaction; Post-inj. 2	47.5	40.4	20.8	
Grade 3 Solicited inj. site reaction	4	3	0	
Grade 3 Solicited inj. site reaction; Post-inj. 1	2	2	0	

Grade 3 Solicited inj. site reaction; Post-inj. 2	2	1	0	
Fever	5.1	2	2	
Fever; Post-inj. 1	1	1	1	
Fever; Post-inj. 2	4	1	1	
Grade 3 Fever	0	1	0	
Grade 3 Fever; Post-inj. 1	0	1	0	
Grade 3 Fever; Post-inj. 2	0	0	0	
Headache	36.4	31	30.7	
Headache; Post-inj. 1	28.3	24	25.7	
Headache; Post-inj. 2	16.2	17.2	12.9	
Grade 3 Headache	1	1	0	
Grade 3 Headache; Post-inj. 1	0	1	0	
Grade 3 Headache; Post-inj. 2	1	0	0	
Malaise	14.1	18	10.9	
Malaise; Post-inj. 1	9.1	15	7.9	
Malaise; Post-inj. 2	7.1	12.1	5.9	
Grade 3 Malaise	2	1	0	
Grade 3 Malaise; Post-inj. 1	1	0	0	
Grade 3 Malaise; Post-inj. 2	1	1	0	
Myalgia	40.4	37	24.8	
Myalgia; Post-inj. 1	33.3	33	16.8	
Myalgia; Post-inj. 2	20.2	19.2	16.8	
Grade 3 Myalgia	1	3	0	
Grade 3 Myalgia; Post-inj. 1	0	2	0	
Grade 3 Myalgia; Post-inj. 2	1	2	0	
Shivering	9.1	19	6.9	
Shivering; Post-inj. 1	3	14	4	
Shivering; Post-inj. 2	6.1	12.1	4	
Grade 3 Shivering	1	2	0	
Grade 3 Shivering; Post-inj. 1	0	1	0	
Grade 3 Shivering; Post-inj. 2	1	1	0	
Solicited systemic reaction	56.6	48	45.5	
Solicited systemic reaction; Post-inj. 1	45.5	43	35.6	
Solicited systemic reaction; Post-inj. 2	30.3	31.3	24.8	
Grade 3 Systemic reaction	2	3	0	
Grade 3 Systemic reaction; Post-inj. 1	1	2	0	
Grade 3 Systemic reaction; Post-inj. 2	1	2	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Elderly Subjects Age Over 60 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 Elderly Subjects Age Over 60 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[35][36]

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: Pain – 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:

[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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
Inj. site Pain	29.6	51	17.8	
Inj. site Pain; Post-inj. 1	16.7	43.1	4.4	
Inj. site Pain; Post-inj. 2	18.5	37.3	15.9	
Grade 3 Inj. site Pain	0	0	0	
Grade 3 Inj. site Pain; Post-inj. 1	0	0	0	
Grade 3 Inj. site Pain; Post-inj. 2	0	0	0	
Inj. site Erythema	5.6	21.6	2.2	
Inj. site Erythema; Post-inj. 1	3.7	15.7	2.2	
Inj. site Erythema; Post-inj. 2	1.9	7.8	0	
Grade 3 Inj. site Erythema	0	0	0	
Grade 3 Inj. site Erythema; Post-inj. 1	0	0	0	
Grade 3 Inj. site Erythema; Post-inj. 2	0	0	0	
Inj. site Swelling	5.6	7.8	0	
Inj. site Swelling; Post-inj. 1	5.6	5.9	0	
Inj. site Swelling; Post-inj. 2	1.9	2	0	
Grade 3 Inj. site Swelling	0	0	0	
Grade 3 Inj. site Swelling; Post-inj. 1	0	0	0	
Grade 3 Inj. site Swelling; Post-inj. 2	0	0	0	
Inj. site Induration	3.7	7.8	0	
Inj. site Induration; Post-inj. 1	1.9	5.9	0	
Inj. site Induration; Post-inj. 2	1.9	2	0	
Grade 3 Inj. site Induration	0	0	0	
Grade 3 Inj. site Induration; Post-inj. 1	0	0	0	
Grade 3 Inj. site Induration; Post-inj. 2	0	0	0	
Inj. site Ecchymosis	1.9	2	2.2	
Inj. site Ecchymosis; Post-inj. 1	1.9	2	0	
Inj. site Ecchymosis; Post-inj. 2	0	0	2.3	
Grade 3 Inj. site Ecchymosis	0	0	0	
Grade 3 Inj. site Ecchymosis; Post-inj. 1	0	0	0	

Grade 3 Inj. site Ecchymosis; Post-inj. 2	0	0	0	
Solicited injection site reaction	35.2	54.9	22.2	
Solicited injection site reaction; Post-inj. 1	20.4	45.1	6.7	
Solicited injection site reaction; Post-inj. 2	20.4	39.2	18.2	
Grade 3 Solicited injection site reaction	0	0	0	
Grade 3 Solicited inj. site reaction; Post-inj. 1	0	0	0	
Grade 3 Solicited inj. site reaction; Post-inj. 2	0	0	0	
Fever	1.9	3.9	0	
Fever; Post-inj. 1	0	3.9	0	
Fever; Post-inj. 2	1.9	0	0	
Grade 3 Fever	0	0	0	
Grade 3 Fever; Post-inj. 1	0	0	0	
Grade 3 Fever; Post-inj. 2	0	0	0	
Headache	14.8	7.8	15.6	
Headache; Post-inj. 1	5.6	5.9	8.9	
Headache; Post-inj. 2	11.1	3.9	11.4	
Grade 3 Headache	0	0	0	
Grade 3 Headache; Post-inj. 1	0	0	0	
Grade 3 Headache; Post-inj. 2	0	0	0	
Malaise	5.6	5.9	8.9	
Malaise; Post-inj. 1	3.7	5.9	8.9	
Malaise; Post-inj. 2	1.9	3.9	0	
Grade 3 Malaise	0	0	0	
Grade 3 Malaise; Post-inj. 1	0	0	0	
Grade 3 Malaise; Post-inj. 2	0	0	0	
Myalgia	7.4	15.7	15.6	
Myalgia; Post-inj. 1	3.7	11.8	11.1	
Myalgia; Post-inj. 2	7.4	5.9	11.4	
Grade 3 Myalgia	0	0	0	
Grade 3 Myalgia; Post-inj. 1	0	0	0	
Grade 3 Myalgia; Post-inj. 2	0	0	0	
Shivering	1.9	7.8	0	
Shivering; Post-inj. 1	0	5.9	0	
Shivering; Post-inj. 2	1.9	3.9	0	
Grade 3 Shivering	0	0	0	
Grade 3 Shivering; Post-inj. 1	0	0	0	
Grade 3 Shivering; Post-inj. 2	0	0	0	
Solicited systemic reaction	18.5	21.6	22.2	
Solicited systemic reaction; Post-inj. 1	9.3	17.6	13.3	
Solicited systemic reaction; Post-inj. 2	13	7.8	18.2	
Grade 3 Solicited systemic reaction	0	0	0	
Grade 3 Solicited systemic reaction; Post-inj. 1	0	0	0	
Grade 3 Solicited systemic reaction; Post-inj. 2	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Adult Subjects Age 18-60 Years Old with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Each Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Adult Subjects Age 18-60 Years Old with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Each Vaccination with Inactivated, Split Virion Swine-origin 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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	100	101	
Units: Percentage of subjects				
number (not applicable)				
Reaction listed in the EMA recommendations	24.2	32	16.8	
Reaction listed in EMA recommendation; Post-inj. 1	16.2	21	12.9	
Reaction listed in EMA recommendation; Post-inj. 2	12.1	20.2	6.9	
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	9.1	5	4	
Inj. site Ecchymosis; Post-inj. 1	5.1	5	2	
Inj. site Ecchymosis; Post-inj. 2	4	0	3	
Pyrexia (temp. >38°C) for 1 day	1	1	0	
Pyrexia (temp. >38°C) for 1 day; Post-inj. 1	0	0	0	
Pyrexia (temp. >38°C) for 1 day; Post-inj. 2	1	1	0	
Malaise	13.1	17	9.9	
Malaise; Post-inj. 1	8.1	12	7.9	
Malaise; Post-inj. 2	7.1	12.1	3	
Shivering	9.1	17	5	

Shivering; Post-inj. 1	3	10	4	
Shivering; Post-inj. 2	6.1	11.1	2	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Elderly Subjects Age Over 60 Years with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Each Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant

End point title	Percentage of Elderly Subjects Age Over 60 Years with at Least One Solicited Reactions Listed in the EMA Note for Guidance Within 3 Days After Each Vaccination with Inactivated, Split Virion Swine-origin A/H1N1 Influenza Vaccine With or Without Adjuvant[39][40]

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 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 study age agroup specified.

End point values	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	51	45	
Units: Percentage of subjects				
number (not applicable)				
Reaction listed in the EMA recommendations	9.3	15.7	6.7	
Reaction listed in EMA recommendation; Post-inj. 1	5.6	13.7	6.7	
Reaction listed in EMA recommendation; Post-inj. 2	3.7	5.9	2.3	
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	5.6	3.9	6.7	
Inj. site Ecchymosis; Post-inj. 1	3.7	3.9	6.7	
Inj. site Ecchymosis; Post-inj. 2	1.9	0	2.3	

Pyrexia (> 38°C) for 1 day	1.9	3.9	0	
Pyrexia (> 38°C) for 1 day; Post-inj. 1	0	3.9	0	
Pyrexia (> 38°C) for 1 day; Post-inj. 2	1.9	0	0	
Malaise	3.7	5.9	2.2	
Malaise; Post-inj. 1	3.7	5.9	2.2	
Malaise; Post-inj. 2	0	3.9	0	
Shivering	1.9	7.8	0	
Shivering; Post-inj. 1	0	5.9	0	
Shivering; Post-inj. 2	1.9	3.9	0	

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 6 months 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; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; 18-60 years
Reporting group description:	
Subjects aged 18-60 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; >60 years
Reporting group description:	
Subjects aged >60 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; >60 years
Reporting group description:	
Subjects aged >60 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; >60 years
Reporting group description:	
Subjects aged >60 years who received two doses of A/H1N1 pandemic influenza vaccine (15 µg HA) 21 days apart.	

Serious adverse events	3.8 µg HA+AF03; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 99 (2.02%)	6 / 100 (6.00%)	7 / 101 (6.93%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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

Bronchial carcinoma			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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
Hodgkin's disease			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (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
Malignant melanoma			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (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
Prostatic adenoma			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (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
Tonsil cancer			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Femoral neck fracture			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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
Open wound			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (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
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular block			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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			
Headache			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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
Sciatica			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	1 / 99 (1.01%)	0 / 100 (0.00%)	0 / 101 (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
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	1 / 101 (0.99%)
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			
Gastrooesphageal reflux disease			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (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
Sigmoiditis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (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
Brief psychotic disorder with marked stressors			
subjects affected / exposed	1 / 99 (1.01%)	0 / 100 (0.00%)	0 / 101 (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
Suicide attempt			

subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	1 / 101 (0.99%)
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 / 100 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 100 (1.00%)	0 / 101 (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
Urinary tract infection			
subjects affected / exposed	0 / 99 (0.00%)	0 / 100 (0.00%)	0 / 101 (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; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 54 (1.85%)	7 / 51 (13.73%)	2 / 45 (4.44%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 45 (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
Bronchial carcinoma			
subjects affected / exposed	0 / 54 (0.00%)	2 / 51 (3.92%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Hodgkin's disease			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Malignant melanoma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 45 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Prostatic adenoma			
subjects affected / exposed	1 / 54 (1.85%)	0 / 51 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Thyroid cancer			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Tonsil cancer			

subjects affected / exposed	1 / 54 (1.85%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 45 (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
Open wound			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular block			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Ischaemic stroke			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 45 (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
Sciatica			

subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesphageal reflux disease			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Sigmoiditis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 45 (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
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Brief psychotic disorder with marked stressors			

subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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
Suicide attempt			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (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 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 45 (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; 18-60 years	7.5 µg HA+AF03; 18-60 years	15 µg HA; 18-60 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 99 (70.71%)	62 / 100 (62.00%)	46 / 101 (45.54%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 99 (36.36%)	31 / 100 (31.00%)	31 / 101 (30.69%)
occurrences (all)	36	31	31
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	69 / 99 (69.70%)	59 / 100 (59.00%)	25 / 101 (24.75%)
occurrences (all)	69	59	25
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 99 (7.07%)	0 / 100 (0.00%)	0 / 101 (0.00%)
occurrences (all)	7	0	0
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 99 (6.06%)	0 / 100 (0.00%)	3 / 101 (2.97%)
occurrences (all)	6	0	3
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 99 (2.02%)	0 / 100 (0.00%)	0 / 101 (0.00%)
occurrences (all)	2	0	0
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 99 (5.05%)	0 / 100 (0.00%)	2 / 101 (1.98%)
occurrences (all)	5	0	2
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 99 (14.14%)	18 / 100 (18.00%)	11 / 101 (10.89%)
occurrences (all)	14	18	11
Shivering			
alternative assessment type: Systematic			

subjects affected / exposed	9 / 99 (9.09%)	19 / 100 (19.00%)	7 / 101 (6.93%)
occurrences (all)	9	19	7
Skin and subcutaneous tissue disorders			
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 99 (7.07%)	9 / 100 (9.00%)	1 / 101 (0.99%)
occurrences (all)	7	9	1
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 99 (40.40%)	37 / 100 (37.00%)	25 / 101 (24.75%)
occurrences (all)	40	37	25

Non-serious adverse events	3.8 µg HA+AF03; >60 years	7.5 µg HA+AF03; >60 years	15 µg HA; >60 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 54 (35.19%)	28 / 51 (54.90%)	10 / 45 (22.22%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	11 / 51 (21.57%)	1 / 45 (2.22%)
occurrences (all)	0	11	1
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	4 / 51 (7.84%)	0 / 45 (0.00%)
occurrences (all)	0	4	0
Injection site ecchymosis			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	1 / 45 (2.22%)
occurrences (all)	0	1	1
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	2 / 51 (3.92%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2010	Included the assessment of the persistence of the immune response at 8 months after the first vaccination in a subset of subjects having received two vaccinations of the vaccines selected for licensure (the 3.8 µg HA + AF03 vaccine and the 15 µg HA without adjuvant vaccine).
27 May 2010	Assessed the potential effect of previous A/H1N1 influenza vaccination on the immune response to the 2010-2011 NH seasonal TIV.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported