Clinical trial results:
Safety and Immunogenicity of an Intramuscular A/H5N1 Inactivated, Split Virion Pandemic Influenza Vaccine in European Children

Summary

EudraCT number	2008-005791-27
Trial protocol	FI
Global end of trial date	18 January 2010

Results information

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

Trial information

Trial identification

Sponsor protocol code	GPA12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00884182
WHO universal trial number (UTN)	-

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 5850, stephanie.pepin@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 4 37 37 5850, 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	30 July 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To describe the safety profiles (injection site reactions and systemic events) during the 21 days following each vaccination in subjects receiving the Day 0-Day 21 and the Day 0-Day 42 vaccination schedules, and 14 days and 21 days after Vaccination 1 and Vaccination 2, respectively, in subjects aged 9 to 17 years receiving the Day 0-Day 14 vaccination schedule
• To describe the immune response 21 days after each vaccination in subjects receiving the Day 0-Day 21 vaccination schedule

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	02 April 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: 350
Worldwide total number of subjects	350
EEA total number of subjects	350

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)	31

Children (2-11 years)	233
Adolescents (12-17 years)	86
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 02 April 2009 to 12 May 2009 in 12 clinical sites in Finland.

Pre-assignment

Screening details:

A total of 350 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	9-17 years (30µg+Ad; D0-D14)

Arm description:

Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 14 days apart.

Arm type	Experimental
Investigational medicinal product name	FLU H5N1 30µgHA+aluminum hydroxide
Investigational medicinal product code	402
Other name	Inactivated split influenza virus A/Indonesia/5/05-RG2 (H5N1)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, Intramuscular (IM) into the deltoid (subjects ≥1 year of age) and thigh (subjects <1 year of age), one dose on Day 0 and Day 14.

Arm title	9-17 years (30µg+Ad; D0-D21)

Arm description:

Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.

Arm type	Experimental
Investigational medicinal product name	FLU H5N1 30µgHA+aluminum hydroxide
Investigational medicinal product code	402
Other name	Inactivated split influenza virus A/Indonesia/5/05-RG2 (H5N1)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, Intramuscular (IM) into the deltoid (subjects ≥1 year of age) and thigh (subjects <1 year of age), one dose on Day 0 and Day 21.

Arm title	9-17 years (30µg+Ad; D0-D42)

Arm description:

Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 42 days apart.

Arm type	Experimental

Investigational medicinal product name	FLU H5N1 30µgHA+aluminum hydroxide
Investigational medicinal product code	402
Other name	Inactivated split influenza virus A/Indonesia/5/05-RG2 (H5N1)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, Intramuscular (IM) into the deltoid (subjects ≥1 year of age) and thigh (subjects <1 year of age), one dose on Day 0 and Day 42.

Arm title	3-8 years (30µg+Ad; D0-D21)

Arm description:

Subjects aged 3-8 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.

Arm type	Experimental
Investigational medicinal product name	FLU H5N1 30µgHA+aluminum hydroxide
Investigational medicinal product code	402
Other name	Inactivated split influenza virus A/Indonesia/5/05-RG2 (H5N1)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, Intramuscular (IM) into the deltoid (subjects ≥1 year of age) and thigh (subjects <1 year of age), one dose on Day 0 and Day 21.

Arm title	6-35 months (30µg+Ad; D0-D21)

Arm description:

Subjects aged 6-35 months who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.

Arm type	Experimental
Investigational medicinal product name	FLU H5N1 30µgHA+aluminum hydroxide
Investigational medicinal product code	402
Other name	Inactivated split influenza virus A/Indonesia/5/05-RG2 (H5N1)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, Intramuscular (IM) into the deltoid (subjects ≥1 year of age) and thigh (subjects <1 year of age), one dose on Day 0 and Day 21.

Number of subjects in period 1	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)
Started	50	50	50
Completed	50	49	48
Not completed	0	1	2
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	1	1
Protocol deviation	-	-	1

Number of subjects in period 1	3-8 years (30µg+Ad; D0-D21)	6-35 months (30µg+Ad; D0-D21)
Started	100	100

Completed	96	96
Not completed	4	4
Consent withdrawn by subject	4	1
Adverse event, non-fatal	-	1
Lost to follow-up	-	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	9-17 years (30µg+Ad; D0-D14)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 14 days apart.	
Reporting group title	9-17 years (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	
Reporting group title	9-17 years (30µg+Ad; D0-D42)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 42 days apart.	
Reporting group title	3-8 years (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 3-8 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	
Reporting group title	6-35 months (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 6-35 months who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	

Reporting group values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)
Number of subjects	50	50	50
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	21	20	23
Adolescents (12-17 years)	29	30	27
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	13	12.8	12.8
standard deviation	± 2.5	± 2.3	± 2.7
Gender categorical Units: Subjects			
Female	33	31	23
Male	17	19	27
Subjects previously vaccinated with an influenza vaccine Units: Subjects			
Yes	4	4	3

No	46	45	45
Unknown	0	1	2
Subjects having experienced influenza-like illness since September 2008 included Units: Subjects			
Yes	8	12	8
No	42	37	42
Unknown	0	1	0

Reporting group values	3-8 years (30µg+Ad; D0-D21)	6-35 months (30µg+Ad; D0-D21)	Total
Number of subjects	100	100	350
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	31	31
Children (2-11 years)	100	69	233
Adolescents (12-17 years)	0	0	86
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	6	2.2	
standard deviation	± 1.5	± 0.6	-
Gender categorical Units: Subjects			
Female	50	55	192
Male	50	45	158
Subjects previously vaccinated with an influenza vaccine Units: Subjects			
Yes	32	65	108
No	68	34	238
Unknown	0	1	4
Subjects having experienced influenza-like illness since September 2008 included Units: Subjects			
Yes	15	10	53
No	83	90	294
Unknown	2	0	3

End points

End points reporting groups

Reporting group title	9-17 years (30µg+Ad; D0-D14)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 14 days apart.	
Reporting group title	9-17 years (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	
Reporting group title	9-17 years (30µg+Ad; D0-D42)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 42 days apart.	
Reporting group title	3-8 years (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 3-8 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	
Reporting group title	6-35 months (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 6-35 months who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	

Primary: Summary of Geometric Mean Titers (GMTs) of Antibody Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Geometric Mean Titers (GMTs) of Antibody Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[1]
End point description:	
Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes 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.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[2]	50	50[3]	100
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	0 (0 to 0)	4 (4 to 4)	0 (0 to 0)	4 (4 to 4)
Day 21	0 (0 to 0)	6.19 (5.11 to 7.5)	0 (0 to 0)	6.37 (5.57 to 7.27)

Day 42	0 (0 to 0)	73.7 (56.4 to 96.4)	0 (0 to 0)	80.6 (65.8 to 98.8)

Notes:

[2] - No vaccine outcome for this group at this time point.

[3] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	4 (4 to 4)			
Day 21	6.26 (5.4 to 7.26)			
Day 42	69.7 (56.7 to 85.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Geometric Mean Titers Ratios (GMTR) Antibody Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Geometric Mean Titers Ratios (GMTR) Antibody Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[4]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes method.

End point type	Primary

End point timeframe:

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

Notes:

[4] - 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.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[5]	50	50[6]	100
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
Day 21/Day 0	0 (0 to 0)	1.55 (1.28 to 1.87)	0 (0 to 0)	1.59 (1.39 to 1.82)
Day 42/Day 21	0 (0 to 0)	11.8 (9.25 to 15.1)	0 (0 to 0)	12.7 (10.7 to 15.2)

Day 42/Day 0	0 (0 to 0)	18.4 (14.1 to 24.1)	0 (0 to 0)	20.2 (16.5 to 24.7)

Notes:

[5] - No vaccine outcome data for this age group at this time point.

[6] - No vaccine outcome data for this age group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
Day 21/Day 0	1.56 (1.35 to 1.81)			
Day 42/Day 21	11.2 (9.39 to 13.4)			
Day 42/Day 0	17.4 (14.2 to 21.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Antibody Titers ≥ 8 (1/dil) or ≥ 32 (1/dil) Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects with Antibody Titers ≥ 8 (1/dil) or ≥ 32 (1/dil) Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[7]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes 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.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[8]	50	50[9]	100
Units: Percentage of subjects				
number (not applicable)				
Day 0; ≥8 (1/dil)	0	0	0	0
Day 21; ≥8 (1/dil)	0	30	0	33
Day 42; ≥8 (1/dil)	0	98	0	98.9

Day 0; ≥32 (1/dil)	0	0	0	0
Day 21; ≥32 (1/dil)	0	6	0	4.3
Day 42; ≥32 (1/dil)	0	87.8	0	90

Notes:

[8] - No vaccine outcome for this group at this time point.

[9] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of subjects				
number (not applicable)				
Day 0; ≥8 (1/dil)	0			
Day 21; ≥8 (1/dil)	30.2			
Day 42; ≥8 (1/dil)	98.9			
Day 0; ≥32 (1/dil)	0			
Day 21; ≥32 (1/dil)	8.3			
Day 42; ≥32 (1/dil)	84.9			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Achieving Seroconversion or Significant Increase in Antibody Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects Achieving Seroconversion or Significant Increase in Antibody Assayed by HI Horse Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[10]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes method. Seroconversion was defined as subjects with pre-vaccination titer <8 (1/dil) and with a post-vaccination titer ≥32 (1/dil) or significant increase was defined as subjects with pre-vaccination titer ≥8 (1/dil) and with at least a 4-fold increase in post-vaccination titer.

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-vaccination

Notes:

[10] - 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.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[11]	50	50[12]	100
Units: Percentage of subjects				
number (not applicable)				
Day 21	0	6	0	4.3
Day 42	0	87.8	0	90

Notes:

[11] - No vaccine outcome for this group at this time point.

[12] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of subjects				
number (not applicable)				
Day 21	8.3			
Day 42	84.9			

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Neutralizing Antibody Geometric Mean Titers (GMTs) Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Neutralizing Antibody Geometric Mean Titers (GMTs) Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[13]

End point description:

Influenza vaccine antibodies were assessed using the seroneutralization method.

End point type	Primary

End point timeframe:

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

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[14]	50	50[15]	100
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				

Day 0	0 (0 to 0)	5 (5 to 5)	0 (0 to 0)	5.04 (4.96 to 5.13)
Day 21	0 (0 to 0)	12.9 (9.52 to 17.4)	0 (0 to 0)	13.2 (10.7 to 16.2)
Day 42	0 (0 to 0)	332 (248 to 444)	0 (0 to 0)	368 (297 to 456)

Notes:

[14] - No vaccine outcome for this group at this time point.

[15] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
Day 0	5 (5 to 5)			
Day 21	12.9 (10.3 to 16.2)			
Day 42	298 (233 to 379)			

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Neutralizing Titers Geometric Mean Titers Ratios (GMTR) of Neutralizing Antibodies Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Neutralizing Titers Geometric Mean Titers Ratios (GMTR) of Neutralizing Antibodies Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[16]

End point description:

Influenza vaccine antibodies were assessed using the seroneutralization method.

End point type	Primary

End point timeframe:

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

Notes:

[16] - 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.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[17]	50	50[18]	100
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				

Day 21/Day 0	0 (0 to 0)	2.57 (1.9 to 3.47)	0 (0 to 0)	2.61 (2.13 to 3.21)
Day 42/Day 21	0 (0 to 0)	25.3 (19.6 to 32.7)	0 (0 to 0)	27.7 (22.8 to 33.7)
Day 42/Day 0	0 (0 to 0)	66.3 (49.5 to 88.9)	0 (0 to 0)	72.9 (58.8 to 90.4)

Notes:

[17] - No vaccine outcome data for this age group at this time point.

[18] - No vaccine outcome data for this age group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
Day 21/Day 0	2.58 (2.06 to 3.24)			
Day 42/Day 21	23.1 (18.8 to 28.4)			
Day 42/Day 0	59.5 (46.7 to 75.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Neutralizing Antibody titers ≥ 10 (1/dil) Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects with Neutralizing Antibody titers ≥ 10 (1/dil) Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[19]

End point description:

Influenza vaccine antibodies were assessed 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.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[20]	50	50[21]	100
Units: Percentage of subjects				
number (not applicable)				
Day 0	0	0	0	1

Day 21	0	52	0	55.1
Day 42	0	100	0	100

Notes:

[20] - No vaccine outcome for this group at this time point.

[21] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of subjects				
number (not applicable)				
Day 0	0			
Day 21	51.5			
Day 42	98.9			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Achieving a 2-fold or 4-fold Increase in Neutralizing Antibody Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects Achieving a 2-fold or 4-fold Increase in Neutralizing Antibody Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine[22]

End point description:

Influenza vaccine antibodies were assessed using the seroneutralization method.

End point type	Primary

End point timeframe:

Day 21 and Day 42 post-vaccination

Notes:

[22] - 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.

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50[23]	50	50[24]	100
Units: Percentage of subjects				
number (not applicable)				
2-fold increase from Day 0 (Day 21)	0	52	0	55.1
2-fold increase from Day 0 (Day 42)	0	100	0	100
4-fold increase from Day 0 (Day 21)	0	32	0	35.7
4-fold increase from Day 0 (Day 42)	0	100	0	98.9

Notes:

[23] - No vaccine outcome for this group at this time point.

[24] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of subjects				
number (not applicable)				
2-fold increase from Day 0 (Day 21)	51.5			
2-fold increase from Day 0 (Day 42)	98.9			
4-fold increase from Day 0 (Day 21)	33			
4-fold increase from Day 0 (Day 42)	97.9			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Geometric Mean Titers (GMTs) of Antibody Assayed by HI Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Geometric Mean Titers (GMTs) of Antibody Assayed by HI Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes method.

End point type	Other pre-specified

End point timeframe:

V01 (pre-vaccination) and V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[25]
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V01	4 (4 to 4)	4 (4 to 4)	4 (4 to 4)	0 (0 to 0)
V02	4.53 (4.07 to 5.05)	6.19 (5.11 to 7.5)	7.77 (6.12 to 9.85)	0 (0 to 0)
V03	50.6 (36.3 to 70.5)	73.7 (56.4 to 96.4)	49.5 (37.5 to 65.4)	0 (0 to 0)

Notes:

[25] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[26]			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V01	0 (0 to 0)			
V02	0 (0 to 0)			
V03	0 (0 to 0)			

Notes:

[26] - No vaccine outcome for this group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Geometric Mean Titers Ratios (GMTR) Antibody Assayed by HI Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Geometric Mean Titers Ratios (GMTR) Antibody Assayed by HI Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes method.

End point type	Other pre-specified

End point timeframe:

V01 (pre-vaccination) and V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[27]
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V02/V01	1.13 (1.02 to 1.26)	1.55 (1.28 to 1.87)	1.94 (1.53 to 2.46)	0 (0 to 0)
V03/V02	11.2 (8.05 to 15.5)	11.8 (9.25 to 15.1)	6.29 (4.94 to 8)	0 (0 to 0)
V03/V01	12.6 (9.07 to 17.6)	18.4 (14.1 to 24.1)	12.4 (9.38 to 16.4)	0 (0 to 0)

Notes:

[27] - No vaccine outcome data for this age group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[28]			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V02/V01	0 (0 to 0)			
V03/V02	0 (0 to 0)			
V03/V01	0 (0 to 0)			

Notes:

[28] - No vaccine outcome data for this age group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Antibody Titers ≥ 8 (1/dil) or ≥ 32 (1/dil) Assayed by HI Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects with Antibody Titers ≥ 8 (1/dil) or ≥ 32 (1/dil) Assayed by HI Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes method.

End point type	Other pre-specified

End point timeframe:

V01 (pre-vaccination) and V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[29]
Units: Percentage of subjects				
number (not applicable)				
V01; ≥8 (1/dil)	0	0	0	0
V02; ≥8 (1/dil)	10	30	42.6	0
V03; ≥8 (1/dil)	92	98	97.8	0
V01; ≥32 (1/dil)	0	0	0	0
V02; ≥32 (1/dil)	2	6	12.8	0
V03; ≥32 (1/dil)	72	87.8	78.3	0

Notes:

[29] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[30]			
Units: Percentage of subjects				
number (not applicable)				
V01; ≥8 (1/dil)	0			
V02; ≥8 (1/dil)	0			
V03; ≥8 (1/dil)	0			
V01; ≥32 (1/dil)	0			
V02; ≥32 (1/dil)	0			
V03; ≥32 (1/dil)	0			

Notes:

[30] - No vaccine outcome for this group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects Achieving Seroconversion or Significant Increase in Antibody Assayed by HI Turkey Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects Achieving Seroconversion or Significant Increase in Antibody Assayed by HI Turkey Erythrocytes Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition using horse erythrocytes method. Seroconversion was defined as subjects with pre-vaccination titer <8 (1/dil) and with a post-vaccination titer ≥32 (1/dil) or significant increase was defined as subjects with pre-vaccination titer ≥8 (1/dil) and with at least a 4-fold increase in post-vaccination titer.

End point type	Other pre-specified

End point timeframe:

V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[31]
Units: Percentage of subjects				
number (not applicable)				
V02	2	6	12.8	0
V03	72	87.8	78.3	0

Notes:

[31] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[32]			
Units: Percentage of subjects				
number (not applicable)				
V02	0			
V03	0			

Notes:

[32] - No vaccine outcome for this group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Geometric Mean Titers (GMTs) of Antibody Assayed Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Geometric Mean Titers (GMTs) of Antibody Assayed Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the seroneutralization method.

End point type	Other pre-specified

End point timeframe:

V01 (pre-vaccination) and V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[33]
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V01	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)	0 (0 to 0)
V02	6.86 (5.61 to 8.38)	12.9 (9.52 to 17.4)	30.7 (22.4 to 42)	0 (0 to 0)
V03	189 (132 to 271)	332 (248 to 444)	303 (230 to 400)	0 (0 to 0)

Notes:

[33] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[34]			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V01	0 (0 to 0)			
V02	0 (0 to 0)			
V03	0 (0 to 0)			

Notes:

[34] - No vaccine outcome for this group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Summary of Geometric Mean Titers Ratios (GMTR) Antibody Assayed by Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Summary of Geometric Mean Titers Ratios (GMTR) Antibody Assayed by Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the seroneutralization method.

End point type	Other pre-specified

End point timeframe:

V01 (pre-vaccination) and V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[35]
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V02/V01	1.37 (1.12 to 1.68)	2.57 (1.9 to 3.47)	6.13 (4.48 to 8.4)	0 (0 to 0)
V03/V02	27.6 (19.2 to 39.7)	25.3 (19.6 to 32.7)	9.66 (7.29 to 12.8)	0 (0 to 0)
V03/V01	37.9 (26.4 to 54.3)	66.3 (49.5 to 88.9)	60.7 (46 to 80)	0 (0 to 0)

Notes:

[35] - No vaccine outcome data for this age group at this time point.

End point values	6-35 months (30µg+Ad; D0-			

	D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[36]			
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
V02/V01	0 (0 to 0)			
V03/V02	0 (0 to 0)			
V03/V01	0 (0 to 0)			

Notes:

[36] - No vaccine outcome data for this age group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Antibody titers ≥10 (1/dil) Assayed by Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects with Antibody titers ≥10 (1/dil) Assayed by Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the seroneutralization method.

End point type	Other pre-specified

End point timeframe:

V01 (pre-vaccination) and V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[37]
Units: Percentage of subjects				
number (not applicable)				
V01	0	0	0	0
V02	20	52	85.4	0
V03	98	100	100	0

Notes:

[37] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[38]			
Units: Percentage of subjects				

number (not applicable)				
V01	0			
V02	0			
V03	0			

Notes:

[38] - No vaccine outcome for this group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with 2- and 4-fold Increase in Antibody titers Assayed by Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects with 2- and 4-fold Increase in Antibody titers Assayed by Seroneutralization Method Against A/Indonesia/5/2005/RG2 (H5N1) Strain Following Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point description:

Influenza vaccine antibodies were assessed using the seroneutralization method.

End point type	Other pre-specified

End point timeframe:

V02 (D14 for subjects on D0-D14 schedule, D21 for D0-D21 schedule, or D42 for D0-D42 schedule) and V03 (D35 for subjects on D0-D14 schedule, D42 for D0-D21 schedule, or D63 for D0-D42 schedule) post-vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100[39]
Units: Percentage of subjects				
number (not applicable)				
2-fold increase from V01 (V02)	20	52	85.4	0
2-fold increase from V01 (V03)	98	100	100	0
4-fold increase from V01 (V02)	10	32	68.8	0
4-fold increase from V01 (V03)	94	100	100	0

Notes:

[39] - No vaccine outcome for this group at this time point.

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	100[40]			
Units: Percentage of subjects				
number (not applicable)				
2-fold increase from V01 (V02)	0			
2-fold increase from V01 (V03)	0			
4-fold increase from V01 (V02)	0			

4-fold increase from V01 (V03)	0			

Notes:

[40] - No vaccine outcome for this group at this time point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects Aged 2 years and over Reporting a Solicited Injection-site or Systemic Reactions Within 7 Days after Injection with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects Aged 2 years and over Reporting a Solicited Injection-site or Systemic Reactions Within 7 Days after Injection with Inactivated Split-Virion, Pandemic Influenza Vaccine

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 – Incapacitating, unable to perform usual activities, may have/or required medical care or absenteeism; Erythema, Swelling, Induration, and Ecchymosis - ≥5 cm. Grade 3 Solicited systemic reactions: Fever - ≥39°C; Headache, Malaise, Myalgia, and Shivering – Prevents daily activities.

End point type	Other pre-specified

End point timeframe:

Day 0 up to Day 7 post-each vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100
Units: Percentage of subjects				
number (not applicable)				
Inj. site Pain; Post-inj. 1	56	65.3	69.4	58.6
Grade 3 Inj. site Pain; Post-inj. 1	0	0	0	0
Inj. site Erythema; Post-inj. 1	30	22.4	24.5	32.3
Grade 3 Inj. site Erythema; Post-inj. 1	0	2	2	2
Inj. site Swelling; Post-inj. 1	10	18.4	10.2	15.2
Grade 3 Inj. site Swelling; Post-inj. 1	2	2	2	0
Inj. site Induration; Post-inj. 1	12	10.2	12.2	23.2
Grade 3 Inj. site Induration; Post-inj. 1	0	0	0	0
Inj. site Ecchymosis; Post-inj. 1	24	16.3	12.2	14.1
Grade 3 Inj. site Ecchymosis; Post-inj. 1	0	0	2	0
Fever; Post-inj. 1	2	8.2	2	4
Grade 3 Fever; Post-inj. 1	0	2	0	0
Headache; Post-inj. 1	38	42.9	38.8	15.2
Grade 3 Headache; Post-inj. 1	2	0	0	0
Malaise; Post-inj. 1	16	34.7	16.3	11.1
Grade 3 Malaise; Post-inj. 1	0	2	0	3
Myalgia; Post-inj. 1	28	44.9	24.5	13.1

Grade 3 Myalgia; Post-inj. 1	0	2	0	0
Shivering; Post-inj. 1	16	16.3	6.1	4
Grade 3 Shivering; Post-inj. 1	0	0	0	0
Inj. site Pain; Post-inj. 2	48	55.1	46.8	56.8
Grade 3 Inj. site Pain; Post-inj. 2	0	2	2.1	1.1
Inj. site Erythema; Post-inj. 2	24	16.3	14.9	25.3
Grade 3 Inj. site Erythema; Post-inj. 2	4	0	2.1	0
Inj. site Swelling; Post-inj. 2	6	14.3	4.3	15.8
Grade 3 Inj. site Swelling; Post-inj. 2	2	0	0	0
Inj. site Induration; Post-inj. 2	16	18.4	6.4	18.9
Grade 3 Inj. site Induration; Post-inj. 2	2	0	0	0
Inj. site Ecchymosis; Post-inj. 2	6	14.3	6.4	10.5
Grade 3 Inj. site Ecchymosis; Post-inj. 2	0	0	2.1	0
Fever; Post-inj. 2	0	0	0	2.1
Grade 3 Fever; Post-inj. 2	0	0	0	0
Headache; Post-inj. 2	28	34.7	21.3	17.9
Grade 3 Headache; Post-inj. 2	0	2	0	0
Malaise; Post-inj. 2	8	26.5	14.9	12.6
Grade 3 Malaise; Post-inj. 2	0	0	0	1.1
Myalgia; Post-inj. 2	20	28.6	17	7.4
Grade 3 Myalgia; Post-inj. 2	0	0	2.1	0
Shivering; Post-inj. 2	12	12.2	2.1	1.1
Grade 3 Shivering; Post-inj. 2	0	0	0	0
Inj. site Pain; Post-any inj.	68	71.4	77.6	73.7
Grade 3 Inj. site Pain; Post-any inj.	0	2	2	1
Inj. site Erythema; Post-any inj.	38	26.5	30.6	43.4
Grade 3 Inj. site Erythema; Post-any inj.	4	2	4.1	2
Inj. site Swelling; Post-any inj.	16	22.4	12.2	21.2
Grade 3 Inj. site Swelling; Post-any inj.	4	2	2	0
Inj. site Induration; Post-any inj.	20	24.5	16.3	33.3
Grade 3 Inj. site Induration; Post-any inj.	2	0	0	0
Inj. site Ecchymosis; Post-any inj.	26	26.5	16.3	20.2
Grade 3 Inj. site Ecchymosis; Post-any inj.	0	0	2	0
Fever; Post-any inj.	2	8.2	2	6.1
Grade 3 Fever; Post-any inj.	0	2	0	0
Headache; Post-any inj.	50	55.1	42.9	24.2
Grade 3 Headache; Post-any inj.	2	2	0	0
Malaise; Post-any inj.	20	44.9	24.5	19.2
Grade 3 Malaise; Post-any inj.	0	2	0	4
Myalgia; Post-any inj.	36	49	32.7	18.2
Grade 3 Myalgia; Post-any inj.	0	2	2	0
Shivering; Post-any inj.	22	22.4	8.2	5.1
Grade 3 Shivering; Post-any inj.	0	0	0	0

End point values	6-35 months (30µg+Ad; D0-D21)			

Subject group type	Reporting group			
Number of subjects analysed	69[41]			
Units: Percentage of subjects				
number (not applicable)				
Inj. site Pain; Post-inj. 1	41.2			
Grade 3 Inj. site Pain; Post-inj. 1	0			
Inj. site Erythema; Post-inj. 1	23.5			
Grade 3 Inj. site Erythema; Post-inj. 1	2.9			
Inj. site Swelling; Post-inj. 1	8.8			
Grade 3 Inj. site Swelling; Post-inj. 1	2.9			
Inj. site Induration; Post-inj. 1	20.6			
Grade 3 Inj. site Induration; Post-inj. 1	0			
Inj. site Ecchymosis; Post-inj. 1	17.6			
Grade 3 Inj. site Ecchymosis; Post-inj. 1	0			
Fever; Post-inj. 1	5.9			
Grade 3 Fever; Post-inj. 1	0			
Headache; Post-inj. 1	8.8			
Grade 3 Headache; Post-inj. 1	0			
Malaise; Post-inj. 1	7.4			
Grade 3 Malaise; Post-inj. 1	1.5			
Myalgia; Post-inj. 1	7.4			
Grade 3 Myalgia; Post-inj. 1	0			
Shivering; Post-inj. 1	2.9			
Grade 3 Shivering; Post-inj. 1	0			
Inj. site Pain; Post-inj. 2	33.3			
Grade 3 Inj. site Pain; Post-inj. 2	0			
Inj. site Erythema; Post-inj. 2	19.7			
Grade 3 Inj. site Erythema; Post-inj. 2	1.5			
Inj. site Swelling; Post-inj. 2	9.1			
Grade 3 Inj. site Swelling; Post-inj. 2	0			
Inj. site Induration; Post-inj. 2	18.2			
Grade 3 Inj. site Induration; Post-inj. 2	1.5			
Inj. site Ecchymosis; Post-inj. 2	9.1			
Grade 3 Inj. site Ecchymosis; Post-inj. 2	0			
Fever; Post-inj. 2	3			
Grade 3 Fever; Post-inj. 2	0			
Headache; Post-inj. 2	6.1			
Grade 3 Headache; Post-inj. 2	0			
Malaise; Post-inj. 2	7.6			
Grade 3 Malaise; Post-inj. 2	0			
Myalgia; Post-inj. 2	7.6			
Grade 3 Myalgia; Post-inj. 2	0			
Shivering; Post-inj. 2	0			
Grade 3 Shivering; Post-inj. 2	0			
Inj. site Pain; Post-any inj.	50			
Grade 3 Inj. site Pain; Post-any inj.	0			
Inj. site Erythema; Post-any inj.	33.8			
Grade 3 Inj. site Erythema; Post-any inj.	4.4			
Inj. site Swelling; Post-any inj.	13.2			
Grade 3 Inj. site Swelling; Post-any inj.	2.9			
Inj. site Induration; Post-any inj.	29.4			

Grade 3 Inj. site Induration; Post-any inj.	1.5			
Inj. site Ecchymosis; Post-any inj.	20.6			
Grade 3 Inj. site Ecchymosis; Post-any inj.	0			
Fever; Post-any inj.	7.4			
Grade 3 Fever; Post-any inj.	0			
Headache; Post-any inj.	11.8			
Grade 3 Headache; Post-any inj.	0			
Malaise; Post-any inj.	11.8			
Grade 3 Malaise; Post-any inj.	1.5			
Myalgia; Post-any inj.	11.8			
Grade 3 Myalgia; Post-any inj.	0			
Shivering; Post-any inj.	2.9			
Grade 3 Shivering; Post-any inj.	0			

Notes:

[41] - Outcome is based on a subset of the subjects aged 24-35 months.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects aged 2 years and over with at Least One Reaction within 3 Days after Any Vaccine Injections listed in the EMEA note for Guidance Following Primary Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

End point title	Percentage of Subjects aged 2 years and over with at Least One Reaction within 3 Days after Any Vaccine Injections listed in the EMEA note for Guidance Following Primary Vaccination with Inactivated Split-Virion, Pandemic Influenza Vaccine

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 one day, Malaise, and Shivering.

End point type	Other pre-specified

End point timeframe:

Day 0 up to Day 3 post-each vaccination

End point values	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)	3-8 years (30µg+Ad; D0-D21)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	100
Units: Percentage of subjects				
number (not applicable)				
At least 1 reaction listed in EMEA	42	57.1	32.7	32.3
At least 1 reaction listed in EMEA; Post-inj. 1	36	42.9	28.6	21.2
At least 1 reaction listed in EMEA; Post-inj. 2	22	36.7	17	17.9
Inj. site induration ≥5 cm for 4 days	0	0	0	0
Inj. site induration ≥5 cm for 4 days; Post-inj. 1	0	0	0	0

Inj. site induration ≥5 cm for 4 days; Post-inj. 2	0	0	0	0
Inj. site ecchymosis	24	24.5	16.3	20.2
Inj. site ecchymosis; Post-inj. 1	22	14.3	12.2	14.1
Inj. site ecchymosis; Post-inj. 2	6	14.3	6.4	10.5
Temperature >38°C (pyrexia) for 1 day	0	0	0	0
Temperature >38°C (pyrexia) for 1 day; Post-inj. 1	0	0	0	0
Temperature >38°C (pyrexia) for 1 day; Post-inj. 2	0	0	0	0
Malaise	14	36.7	20.4	15.2
Malaise; Post-inj. 1	8	24.5	12.2	8.1
Malaise; Post-inj. 2	8	22.4	10.6	8.4
Shivering	20	22.4	8.2	4
Shivering; Post-inj. 1	14	16.3	6.1	3
Shivering; Post-inj. 2	12	10.2	2.1	1.1

End point values	6-35 months (30µg+Ad; D0-D21)			
Subject group type	Reporting group			
Number of subjects analysed	69[42]			
Units: Percentage of subjects				
number (not applicable)				
At least 1 reaction listed in EMEA	32.4			
At least 1 reaction listed in EMEA; Post-inj. 1	23.5			
At least 1 reaction listed in EMEA; Post-inj. 2	16.7			
Inj. site induration ≥5 cm for 4 days	0			
Inj. site induration ≥5 cm for 4 days; Post-inj. 1	0			
Inj. site induration ≥5 cm for 4 days; Post-inj. 2	0			
Inj. site ecchymosis	19.1			
Inj. site ecchymosis; Post-inj. 1	14.7			
Inj. site ecchymosis; Post-inj. 2	9.1			
Temperature >38°C (pyrexia) for 1 day	15			
Temperature >38°C (pyrexia) for 1 day; Post-inj. 1	1.5			
Temperature >38°C (pyrexia) for 1 day; Post-inj. 2	0			
Malaise	11.8			
Malaise; Post-inj. 1	7.4			
Malaise; Post-inj. 2	7.6			
Shivering	2.9			
Shivering; Post-inj. 1	2.9			
Shivering; Post-inj. 2	0			

Notes:

[42] - Outcome is based on a subset of the subjects aged 24-35 months.

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	11.0

Reporting groups	
Reporting group title	9-17 years (30µg+Ad; D0-D14)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 14 days apart.	
Reporting group title	9-17 years (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	
Reporting group title	9-17 years (30µg+Ad; D0-D42)
Reporting group description:	
Subjects aged 9-17 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 42 days apart.	
Reporting group title	3-8 years (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 3-8 years who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	
Reporting group title	6-35 months (30µg+Ad; D0-D21)
Reporting group description:	
Subjects aged 6-35 months who received two intramuscular administrations of the 30µg HA+aluminum hydroxide vaccine 21 days apart.	

Serious adverse events	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (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
Gastrointestinal disorders			
Appendicitis perforated			

subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (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
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	3-8 years (30µg+Ad; D0-D21)	6-35 months (30µg+Ad; D0-D21)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Appendicitis perforated			

subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	9-17 years (30µg+Ad; D0-D14)	9-17 years (30µg+Ad; D0-D21)	9-17 years (30µg+Ad; D0-D42)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 50 (68.00%)	35 / 50 (70.00%)	38 / 50 (76.00%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[1]	25 / 50 (50.00%)	27 / 49 (55.10%)	21 / 49 (42.86%)
occurrences (all)	25	27	21
General disorders and administration site conditions			

Injection site pruritus			
subjects affected / exposed[2]	1 / 50 (2.00%)	2 / 50 (4.00%)	0 / 49 (0.00%)
occurrences (all)	1	2	0
Irritability			
subjects affected / exposed[3]	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed[4]	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 49 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[5]	34 / 50 (68.00%)	35 / 49 (71.43%)	38 / 49 (77.55%)
occurrences (all)	34	35	38
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[6]	19 / 50 (38.00%)	13 / 49 (26.53%)	15 / 49 (30.61%)
occurrences (all)	19	13	15
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[7]	8 / 50 (16.00%)	11 / 49 (22.45%)	6 / 49 (12.24%)
occurrences (all)	8	11	6
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[8]	13 / 50 (26.00%)	13 / 49 (26.53%)	8 / 49 (16.33%)
occurrences (all)	13	13	8
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[9]	1 / 50 (2.00%)	4 / 49 (8.16%)	1 / 49 (2.04%)
occurrences (all)	1	4	1
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[10]	10 / 50 (20.00%)	22 / 49 (44.90%)	12 / 49 (24.49%)
occurrences (all)	10	22	12
Shivering			
alternative assessment type: Systematic			

subjects affected / exposed[11]	11 / 50 (22.00%)	11 / 49 (22.45%)	4 / 49 (8.16%)
occurrences (all)	11	11	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[12]	0 / 50 (0.00%)	1 / 50 (2.00%)	1 / 49 (2.04%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed[13]	2 / 50 (4.00%)	5 / 50 (10.00%)	1 / 49 (2.04%)
occurrences (all)	2	5	1
Pharyngolaryngeal pain			
subjects affected / exposed[14]	2 / 50 (4.00%)	5 / 50 (10.00%)	1 / 49 (2.04%)
occurrences (all)	2	5	1
Skin and subcutaneous tissue disorders			
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[15]	10 / 50 (20.00%)	12 / 49 (24.49%)	8 / 49 (16.33%)
occurrences (all)	10	12	8
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[16]	18 / 50 (36.00%)	24 / 49 (48.98%)	16 / 49 (32.65%)
occurrences (all)	18	24	16
Infections and infestations			
Gastroenteritis			
subjects affected / exposed[17]	1 / 50 (2.00%)	4 / 50 (8.00%)	2 / 49 (4.08%)
occurrences (all)	1	4	2
Nasopharyngitis			
subjects affected / exposed[18]	2 / 50 (4.00%)	2 / 50 (4.00%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
Otitis media			
subjects affected / exposed[19]	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed[20]	3 / 50 (6.00%)	1 / 50 (2.00%)	1 / 49 (2.04%)
occurrences (all)	3	1	1

Upper respiratory tract infection			
subjects affected / exposed[21]	1 / 50 (2.00%)	4 / 50 (8.00%)	4 / 49 (8.16%)
occurrences (all)	1	4	4

Non-serious adverse events	3-8 years (30µg+Ad; D0-D21)	6-35 months (30µg+Ad; D0-D21)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 100 (73.00%)	34 / 100 (34.00%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[1]	24 / 99 (24.24%)	8 / 68 (11.76%)	
occurrences (all)	24	8	
General disorders and administration site conditions			
Injection site pruritus			
subjects affected / exposed[2]	5 / 99 (5.05%)	2 / 98 (2.04%)	
occurrences (all)	5	2	
Irritability			
subjects affected / exposed[3]	0 / 99 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	6	
Pyrexia			
subjects affected / exposed[4]	4 / 99 (4.04%)	11 / 98 (11.22%)	
occurrences (all)	4	11	
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[5]	73 / 99 (73.74%)	34 / 68 (50.00%)	
occurrences (all)	73	34	
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[6]	43 / 99 (43.43%)	23 / 68 (33.82%)	
occurrences (all)	43	23	
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[7]	21 / 99 (21.21%)	9 / 68 (13.24%)	
occurrences (all)	21	9	
Injection site ecchymosis			
alternative assessment type: Systematic			

subjects affected / exposed[8]	20 / 99 (20.20%)	14 / 68 (20.59%)	
occurrences (all)	20	14	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[9]	6 / 99 (6.06%)	5 / 68 (7.35%)	
occurrences (all)	6	5	
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[10]	19 / 99 (19.19%)	8 / 68 (11.76%)	
occurrences (all)	19	8	
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[11]	5 / 99 (5.05%)	2 / 68 (2.94%)	
occurrences (all)	5	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[12]	1 / 99 (1.01%)	8 / 98 (8.16%)	
occurrences (all)	1	8	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed[13]	14 / 99 (14.14%)	17 / 98 (17.35%)	
occurrences (all)	14	17	
Pharyngolaryngeal pain			
subjects affected / exposed[14]	8 / 99 (8.08%)	0 / 98 (0.00%)	
occurrences (all)	8	0	
Skin and subcutaneous tissue disorders			
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[15]	33 / 99 (33.33%)	20 / 68 (29.41%)	
occurrences (all)	33	20	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[16]	18 / 99 (18.18%)	8 / 68 (11.76%)	
occurrences (all)	18	8	

Infections and infestations			
Gastroenteritis			
subjects affected / exposed[17]	6 / 99 (6.06%)	6 / 98 (6.12%)	
occurrences (all)	6	6	
Nasopharyngitis			
subjects affected / exposed[18]	5 / 99 (5.05%)	5 / 98 (5.10%)	
occurrences (all)	5	5	
Otitis media			
subjects affected / exposed[19]	1 / 99 (1.01%)	7 / 98 (7.14%)	
occurrences (all)	1	7	
Rhinitis			
subjects affected / exposed[20]	19 / 99 (19.19%)	22 / 98 (22.45%)	
occurrences (all)	19	22	
Upper respiratory tract infection			
subjects affected / exposed[21]	6 / 99 (6.06%)	10 / 98 (10.20%)	
occurrences (all)	6	10	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an solicited adverse event recorded in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an solicited adverse event recorded in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an solicited adverse event recorded in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an solicited adverse event recorded in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an solicited adverse event that were spontaneously reported in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an solicited adverse event recorded in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an solicited adverse event recorded in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an solicited adverse event recorded in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an solicited adverse event that were spontaneously reported in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an solicited adverse event recorded in a diary card within 7 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[18] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[19] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects

for which the diary cards were returned and for which data were available for the event during the period.
[20] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[21] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was an unsolicited adverse event that were spontaneously reported in a diary card within 21 days after each vaccination; therefore, the total number (N) of subjects reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported