Clinical trial results:
A Phase II, Randomized, Controlled, Observer-blind, Single-center Study to Evaluate the Immunogenicity, Safety and Tolerability of Two Doses of FLUAD-H5N1 Influenza Vaccine in Subjects aged 6 months to 17 years

Summary

EudraCT number	2007-002480-27
Trial protocol	FI
Global end of trial date	18 May 2009

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	04 February 2015
Version creation reason	• Correction of full data set Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required. Moreover, a change in system user for this study is necessary.

Trial information

Trial identification

Sponsor protocol code	V87P6

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00537524
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics GmbH & Co. KG
Sponsor organisation address	Emil-von-Behring-Strasse 76, Marburg, Germany, 35006
Public contact	Posting Director, Novartis Vaccines and Diagnostics GmbH & Co. KG, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics GmbH & Co. KG, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000663-PIP01-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 August 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 May 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the magnitude of antibody responses to two doses of MF59-PanH5N1 influenza vaccine, each containing 7.5µg of H5N1 antigen administered 3 weeks apart in subjects of different ages.

Protection of trial subjects:

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

Standard immunization practices should be observed and care should be taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision should be readily available in case of anaphylactic reactions following administration of the study vaccine, in accordance with local practice/guidelines such as epinephrine 1:1000 and diphenhydramine.

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines. An oral temperature ≥38.0°C (≥100.4°F) or serious active infection was a reason for delaying vaccination. Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	11 September 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 472
Worldwide total number of subjects	472
EEA total number of subjects	472

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)	134
Children (2-11 years)	247
Adolescents (12-17 years)	91
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at one study center in Finland.

Pre-assignment

Screening details:

All subjects enrolled were included in the trial, except for one subject whose parent/guardian withdrew of consent on day 1.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	MF59-PANH5N1 IV (6 to <36months)

Arm description:

Toddlers received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose

Arm type	Experimental
Investigational medicinal product name	MF59-PanH5N1 IV vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.5 mL doses of H5N1 influenza vaccine and one 0.5 mL dose of H5N1 vaccine administered IM in the left deltoid or anterolateral thigh

Arm title	MF59-PANH5N1 IV (3 to <9 years)

Arm description:

Children received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose

Arm type	Experimental
Investigational medicinal product name	MF59-PanH5N1 IV vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.5 mL doses of H5N1 influenza vaccine and one 0.5 mL dose of H5N1 vaccine administered IM in the left deltoid or anterolateral thigh

Arm title	MF59-PANH5N1 IV (9 to <18 years)

Arm description:

Adolescents received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose

Arm type	Experimental

Investigational medicinal product name	MF59-PanH5N1 IV vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.5 mL doses of H5N1 influenza vaccine and one 0.5 mL dose of H5N1 vaccine administered IM in the left deltoid or anterolateral thigh

Arm title	MF59-Seasonal IV (6 to <36months)

Arm description:

Toddlers received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart

Arm type	Active comparator
Investigational medicinal product name	MF59-Seasonal IV vaccine
Investigational medicinal product code	
Other name	Fluad
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.25mL or 0.5mL doses of H5N1 influenza vaccine administered IM in the left deltoid or anterolateral thigh

Arm title	MF59-Seasonal IV (3 to <9 years)

Arm description:

Children received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart

Arm type	Active comparator
Investigational medicinal product name	MF59-Seasonal IV vaccine
Investigational medicinal product code	
Other name	Fluad
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.25mL or 0.5mL doses of H5N1 influenza vaccine administered IM in the left deltoid or anterolateral thigh

Arm title	MF59-Seasonal IV (9 to <18 years)

Arm description:

Adolescents received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart

Arm type	Active comparator
Investigational medicinal product name	MF59-Seasonal IV vaccine
Investigational medicinal product code	
Other name	Fluad
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.25mL or 0.5mL doses of H5N1 influenza vaccine administered IM in the left deltoid or anterolateral thigh

Number of subjects in period 1	MF59-PANH5N1 IV (6 to <36months)	MF59-PANH5N1 IV (3 to <9 years)	MF59-PANH5N1 IV (9 to <18 years)
Started	145	96	94
Completed	122	84	83
Not completed	23	12	11
Adverse event, serious fatal	1	2	-
Consent withdrawn by subject	16	8	6
Unable to classify	1	-	1
Lost to follow-up	5	2	3
Protocol deviation	-	-	1

Number of subjects in period 1	MF59-Seasonal IV (6 to <36months)	MF59-Seasonal IV (3 to <9 years)	MF59-Seasonal IV (9 to <18 years)
Started	56	40	41
Completed	56	38	40
Not completed	0	2	1
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	-	1
Unable to classify	-	-	-
Lost to follow-up	-	1	-
Protocol deviation	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	MF59-PANH5N1 IV (6 to <36months)
Reporting group description:	
Toddlers received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-PANH5N1 IV (3 to <9 years)
Reporting group description:	
Children received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-PANH5N1 IV (9 to <18 years)
Reporting group description:	
Adolescents received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-Seasonal IV (6 to <36months)
Reporting group description:	
Toddlers received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart	
Reporting group title	MF59-Seasonal IV (3 to <9 years)
Reporting group description:	
Children received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart	
Reporting group title	MF59-Seasonal IV (9 to <18 years)
Reporting group description:	
Adolescents received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart	

Reporting group values	MF59-PANH5N1 IV (6 to <36months)	MF59-PANH5N1 IV (3 to <9 years)	MF59-PANH5N1 IV (9 to <18 years)
Number of subjects	145	96	94
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)	96	0	0
Children (2-11 years)	49	96	31
Adolescents (12-17 years)	0	0	63
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	19.1	5.5	13
standard deviation	± 8.7	± 1.7	± 2.7
Gender categorical Units: Subjects			
Female	78	44	57
Male	67	52	37

Reporting group values	MF59-Seasonal IV (6 to <36months)	MF59-Seasonal IV (3 to <9 years)	MF59-Seasonal IV (9 to <18 years)
Number of subjects	56	40	41
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)	38	0	0
Children (2-11 years)	18	40	13
Adolescents (12-17 years)	0	0	28
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: months			
arithmetic mean	18.7	5.5	13
standard deviation	± 9.1	± 1.6	± 2.7
Gender categorical			
Units: Subjects			
Female	29	13	20
Male	27	27	21

Reporting group values	Total		
Number of subjects	472		
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)	134		
Children (2-11 years)	247		
Adolescents (12-17 years)	91		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	241		
Male	231		

End points

End points reporting groups

Reporting group title	MF59-PANH5N1 IV (6 to <36months)
Reporting group description:	
Toddlers received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-PANH5N1 IV (3 to <9 years)
Reporting group description:	
Children received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-PANH5N1 IV (9 to <18 years)
Reporting group description:	
Adolescents received two doses 0.5 mL of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-Seasonal IV (6 to <36months)
Reporting group description:	
Toddlers received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart	
Reporting group title	MF59-Seasonal IV (3 to <9 years)
Reporting group description:	
Children received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart	
Reporting group title	MF59-Seasonal IV (9 to <18 years)
Reporting group description:	
Adolescents received two 0.25mL or 0.5mL doses of H5N1 influenza vaccine, administered 3 weeks apart	
Subject analysis set title	Full Analysis Population (HI)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the enrolled population who actually received a study vaccination, and provided at least one evaluable serum sample at post baseline.	
Subject analysis set title	Full Analysis Population (SRH, MN)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the enrolled population who actually received a study vaccination, and provided at least one evaluable serum sample at post baseline.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the Exposed population who provided post vaccination and post-baseline safety data.	

Primary: Percentages of subjects with HI titers ≥ 40 after primary vaccination in toddlers-FAS

End point title	Percentages of subjects with HI titers ≥ 40 after primary vaccination in toddlers-FAS[1][2]
End point description:	
The immune response was measured as the percentage of subjects with HI titers ≥40 after primary vaccination, as defined by CHMP (MF59-PanH5N1 IV) against HI Strain H5N1 A/Vietnam administered 3 weeks apart in toddlers.	
End point type	Primary
End point timeframe:	
Day 1 and Day 43	

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (6 to <36months)	MF59-Seasonal IV (6 to <36months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	55		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 1 (N=134,55)	1 (0.019 to 4)	0 (0 to 6)		
Day 43 (N=131,54)	97 (92 to 99)	0 (0 to 7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with HI titers ≥ 40 after primary vaccination in children-FAS

End point title	Percentages of subjects with HI titers ≥ 40 after primary vaccination in children-FAS[3][4]

End point description:

The immune response was measured as the percentage of subjects with HI titers ≥40 after primary vaccination, as defined by CHMP (MF59-PanH5N1 IV) against HI Strain H5N1 A/Vietnam administered 3 weeks apart in children

End point type	Primary

End point timeframe:

Day 1 and Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (3 to <9 years)	MF59-Seasonal IV (3 to <9 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	40		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 1 (N=91,40)	0 (0 to 4)	0 (0 to 9)		
Day 43 (N=91,39)	97 (91 to 99)	0 (0 to 9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with HI titers ≥ 40 after primary vaccination in adolescents-FAS

End point title	Percentages of subjects with HI titers ≥ 40 after primary vaccination in adolescents-FAS[5][6]

End point description:

The immune response was measured as the percentage of subjects with HI titers ≥40 after primary vaccination, as defined by CHMP (MF59-PanH5N1 IV) against HI Strain H5N1 A/Vietnam administered 3 weeks apart in adolescents.

End point type	Primary

End point timeframe:

Day 1 and Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (9 to <18 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	40		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 1 (N=89,40)	1 (0.028 to 6)	0 (0 to 9)		
Day 43 (N=89,40)	89 (80 to 94)	0 (0 to 9)		

Statistical analyses

No statistical analyses for this end point

Primary: The geometric mean titers (GMTs) determined by HI assay after primary vaccination in toddlers-FAS

End point title	The geometric mean titers (GMTs) determined by HI assay after primary vaccination in toddlers-FAS[7][8]

End point description:

The immune response was measured as the geometric mean bactericidal titers directed against HI Strain H5N1 A/Vietnam administered 3 weeks apart in toddlers.

End point type	Primary

End point timeframe:

Day 1 and Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (6 to <36months)	MF59-Seasonal IV (6 to <36months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	55		
Units: Titer				
geometric mean (confidence interval 95%)				
Day 1 (N=134,55)	5.12 (4.92 to 5.32)	5.01 (4.71 to 5.32)		
Day 43 (N=131,54)	658 (560 to 773)	5.03 (3.91 to 6.47)		

Statistical analyses

No statistical analyses for this end point

Primary: The geometric mean titers (GMTs) determined by HI assay after primary vaccination in children-FAS

End point title	The geometric mean titers (GMTs) determined by HI assay after primary vaccination in children-FAS[9][10]

End point description:

The immune response was measured as the geometric mean bactericidal titers directed against HI Strain H5N1 A/Vietnam administered 3 weeks apart in children

End point type	Primary

End point timeframe:

Day 1 and Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (3 to <9 years)	MF59-Seasonal IV (3 to <9 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	40		
Units: Titer				
geometric mean (confidence interval 95%)				
Day 1 (N=91,40)	5 (5 to 5)	5 (5 to 5)		
Day 43 (N=91,39)	585 (484 to 708)	4.93 (3.68 to 6.6)		

Statistical analyses

No statistical analyses for this end point

Primary: The geometric mean titers (GMTs) determined by HI assay after primary vaccination in adolescents-FAS

End point title	The geometric mean titers (GMTs) determined by HI assay after primary vaccination in adolescents-FAS[11][12]

End point description:

The immune response was measured as the geometric mean bactericidal titers directed against HI Strain H5N1 A/Vietnam administered 3 weeks apart in adolescents

End point type	Primary

End point timeframe:

Day 1 and Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (9 to <18 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	40		
Units: Titer				
geometric mean (confidence interval 95%)				
Day 1 (N=89,40)	5.15 (4.95 to 5.43)	5.01 (4.64 to 5.4)		
Day 43 (N=89,40)	344 (261 to 453)	5.07 (3.36 to 7.65)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination in toddlers-FAS

End point title	Percentages of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination in toddlers-FAS[13][14]

End point description:

The immune response was measured as the percentage of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination, as defined by CHMP (MF59-PanH5N1 IV) against HI Strain H5N1 A/Vietnam administered 3 weeks apart in toddlers.

End point type	Primary

End point timeframe:

Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (6 to <36months)	MF59-Seasonal IV (6 to <36months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	55		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 43 (N-131, 54)	97 (92 to 99)	0 (0 to 7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination in children-FAS

End point title	Percentages of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination in children-FAS[15][16]

End point description:

The immune response was measured as the percentage of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination, as defined by CHMP (MF59-PanH5N1 IV) against HI Strain H5N1 A/Vietnam administered 3 weeks apart in children

End point type	Primary

End point timeframe:

Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (3 to <9 years)	MF59-Seasonal IV (3 to <9 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	40		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 43 (N=91,39)	97 (91 to 99)	0 (0 to 9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination in adolescents-FAS

End point title	Percentages of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination in adolescents-FAS[17][18]

End point description:

The immune response was measured as the percentage of subjects with Seroconversion or Significant increase from day 1 in HI titers after primary vaccination, as defined by CHMP (MF59-PanH5N1 IV) against HI Strain H5N1 A/Vietnam administered 3 weeks apart in adolescents

End point type	Primary

End point timeframe:

Day 43

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: There were no statistical analysis done.

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (9 to <18 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	40		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 43 (N=89,40)	89 (80 to 94)	0 (0 to 9)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting solicited local and systemic adverse events after receiving 2 doses of MF59-PanH5N1 IV vaccine

End point title	Number of subjects reporting solicited local and systemic adverse events after receiving 2 doses of MF59-PanH5N1 IV vaccine[19]

End point description:

The safety and tolerability of the 2 doses of MF59-PanH5N1 IV vaccine administered 3 weeks apart in subjects (all age groups) according to different schedules is reported as number of subjects with solicited local* and systemic adverse events.

End point type	Primary

End point timeframe:

From day 1 to day 7 after 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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (6 to <36months)	MF59-PANH5N1 IV (3 to <9 years)	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (6 to <36months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	138	93	91	56
Units: Percentage of subjects				
Any (vaccination 2)	68	68	82	63
Any local (vaccination 2)	46	58	70	41
Any systemic (vaccination 2)	51	33	52	46
Any Other (vaccination 2)	16	12	15	20

End point values	MF59-Seasonal IV (3 to <9 years)	MF59-Seasonal IV (9 to <18 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: Percentage of subjects				
Any (vaccination 2)	56	78		
Any local (vaccination 2)	49	65		
Any systemic (vaccination 2)	36	50		
Any Other (vaccination 2)	15	8		

Statistical analyses

No statistical analyses for this end point

Secondary: The geometric mean titers (GMTs) determined by HI assay after booster vaccinations in MF59-PanH5N1 IV in toddlers-FAS

End point title	The geometric mean titers (GMTs) determined by HI assay after booster vaccinations in MF59-PanH5N1 IV in toddlers-FAS[20]

End point description:

The immune response was measured as the geometric mean bactericidal titers directed against HI Strain H5N1 A/Vietnam following 12 month booster dose in toddlers

End point type	Secondary

End point timeframe:

Day 382 and Day 403

Notes:

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (6 to <36months)			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Titer				
geometric mean (confidence interval 95%)				
Day 382 (N=113) Day 403 (N=113)	25 (18 to 34) 1365 (1166 to 1598)			

Statistical analyses

No statistical analyses for this end point

Secondary: The geometric mean titers (GMTs) determined by HI assay after booster vaccinations in MF59-PanH5N1 IV in children-FAS

End point title	The geometric mean titers (GMTs) determined by HI assay after booster vaccinations in MF59-PanH5N1 IV in children-FAS[21]

End point description:

The immune response was measured as the geometric mean bactericidal titers directed against HI Strain H5N1 A/Vietnam following 12 month booster dose in children

End point type	Secondary

End point timeframe:

Day 382 and Day 403

Notes:

[21] - 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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (3 to <9 years)			
Subject group type	Reporting group			
Number of subjects analysed	83			
Units: Titer				
geometric mean (confidence interval 95%)				
Day 382 (N=83) Day 403 (N=83)	10 (7.93 to 14) 766 (613 to 958)			

Statistical analyses

No statistical analyses for this end point

Secondary: The geometric mean titers (GMTs) determined by HI assay after booster vaccinations in MF59-PanH5N1 IV in adolescents-FAS

End point title	The geometric mean titers (GMTs) determined by HI assay after booster vaccinations in MF59-PanH5N1 IV in adolescents-FAS[22]

End point description:

The immune response was measured as the geometric mean bactericidal titers directed against HI Strain H5N1 A/Vietnam following 12 month booster dose in adolescents

End point type	Secondary

End point timeframe:

Day 382 and Day 403

Notes:

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (9 to <18 years)			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Titer				
geometric mean (confidence interval 95%)				
Day 383 (N=81) Day 403 (N=81)	12 (8.92 to 16) 472 (335 to 667)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects Showing Seroprotection (CHMP) by SRH Assay (MF59-PanH5N1 IV) in toddlers-FAS

End point title	Percentage of subjects Showing Seroprotection (CHMP) by SRH Assay (MF59-PanH5N1 IV) in toddlers-FAS[23]

End point description:

Evaluate cross-protection of MF59-PanH5N1 IV in toddlers-FAS persistence population

End point type	Secondary

End point timeframe:

Day 1 and Day 382

Notes:

[23] - 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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (6 to <36months)			
Subject group type	Reporting group			
Number of subjects analysed	122			
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 1 (N=122)	3 (1 to 8)			

Day 382 (N=122)	88 (81 to 93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects Showing Seroprotection (CHMP) by SRH Assay (MF59-PanH5N1 IV) in children-FAS

End point title	Percentage of subjects Showing Seroprotection (CHMP) by SRH Assay (MF59-PanH5N1 IV) in children-FAS[24]

End point description:

Evaluate cross-protection of MF59-PanH5N1 IV in children-FAS persistence population

End point type	Secondary

End point timeframe:

Day 1 and 382

Notes:

[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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (3 to <9 years)			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 1 (N=85)	0 (0 to 4)			
Day 382 (N=85)	71 (60 to 80)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects Showing Seroprotection (CHMP) by SRH Assay (MF59-PanH5N1 IV) in adolescents-FAS

End point title	Percentage of subjects Showing Seroprotection (CHMP) by SRH Assay (MF59-PanH5N1 IV) in adolescents-FAS[25]

End point description:

Evaluate cross-protection of MF59-PanH5N1 IV in adolescents-FAS persistence population

End point type	Secondary

End point timeframe:

Day 1 and 382

Notes:

[25] - 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: There were no statistical analysis done.

End point values	MF59-PANH5N1 IV (9 to <18 years)			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: Percentage of subjects				
number (confidence interval 95%)				
Day 1 (N=82) Day 382 (N=82)	5 (1 to 12) 61 (50 to 72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local and systemic adverse events after receiving one dose of MF59-PanH5N1 IV vaccine after 12 months of 2nd dose

End point title	Number of subjects reporting solicited local and systemic adverse events after receiving one dose of MF59-PanH5N1 IV vaccine after 12 months of 2nd dose

End point description:

The safety and tolerability of the 1 dose of MF59-PanH5N1 IV vaccine administered 12 months after 2nd dose in subjects (all age groups) according to different schedules is reported as number of subjects with solicited local* and systemic adverse events.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after vaccination

End point values	MF59-PANH5N1 IV (6 to <36months)	MF59-PANH5N1 IV (3 to <9 years)	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (6 to <36months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	85	83	0[26]
Units: Percentage of subjects				
Any (vaccination 3)	80	79	89	
Any local (vaccination 3)	60	74	81	
Any Systemic (vaccination 3)	54	45	69	
Any other (vaccination 3)	19	14	16	

Notes:

[26] - Booster dose not given for the active comparator cohort

End point values	MF59-Seasonal IV (3 to <9 years)	MF59-Seasonal IV (9 to <18 years)		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[27]	0[28]		
Units: Percentage of subjects				
Any (vaccination 3) Any local (vaccination 3) Any Systemic (vaccination 3) Any other (vaccination 3)				

Notes:

[27] - Booster dose not given for the active comparator cohort

[28] - Booster dose not given for the active comparator cohort

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited local and systemic adverse events after receiving one dose of MF59-PanH5N1 IV vaccine after 12 months of 2nd dose

End point title	Number of subjects reporting unsolicited local and systemic adverse events after receiving one dose of MF59-PanH5N1 IV vaccine after 12 months of 2nd dose

End point description:

End point type	Secondary

End point timeframe:

From day 1 to day 21 after vaccination

End point values	MF59-PANH5N1 IV (6 to <36months)	MF59-PANH5N1 IV (3 to <9 years)	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (6 to <36months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	85	83	0[29]
Units: Percentage of subjects				
Any AEs	23	12	8	
At least possibly related AEs	0	0	0	
Serious AEs	2	0	0	
AEs leading to discontinuation	0	0	0	

Notes:

[29] - Booster dose not given to the active comparator cohort

End point values	MF59-Seasonal IV (3 to <9 years)	MF59-Seasonal IV (9 to <18 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	0[31]		
Units: Percentage of subjects				
Any AEs At least possibly related AEs Serious AEs AEs leading to discontinuation				

Notes:
[30] - Booster dose not given to the active comparator cohort
[31] - Booster dose not given to the active comparator cohort

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout the study period (day 1 to after primary vaccination after a 12 month booster vaccination)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	MF59-PANH5N1 IV (3 to <9 years)
Reporting group description:	
Children received two doses 0.5 ml of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-PANH5N1 IV (9 to <18 years)
Reporting group description:	
Adolescents received two doses 0.5 ml of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-Seasonal IV (6 to <36months)
Reporting group description:	
Toddlers received two doses 0.5 ml of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-Seasonal IV (3 to <9 years)
Reporting group description:	
Children received two doses 0.5 ml of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-Seasonal IV (9 to <18 years)
Reporting group description:	
Adolescents received two doses 0.5 ml of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	
Reporting group title	MF59-PANH5N1 IV (6 to <36months)
Reporting group description:	
Toddlers received two doses 0.5 ml of H5N1 influenza vaccine, administered 3 weeks apart, and one dose of H5N1 vaccine 12 months after the second dose	

Serious adverse events	MF59-PANH5N1 IV (3 to <9 years)	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (6 to <36months)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 96 (3.13%)	3 / 93 (3.23%)	2 / 56 (3.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Forearm fracture			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic renal injury			
subjects affected / exposed	1 / 96 (1.04%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Immune thrombocytopenic purpura			
subjects affected / exposed	1 / 96 (1.04%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 96 (1.04%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 96 (0.00%)	1 / 93 (1.08%)	0 / 56 (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
Volvulus			

subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 96 (0.00%)	1 / 93 (1.08%)	0 / 56 (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
Major depression			
subjects affected / exposed	0 / 96 (0.00%)	1 / 93 (1.08%)	0 / 56 (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
Mental disorder			
subjects affected / exposed	0 / 96 (0.00%)	1 / 93 (1.08%)	0 / 56 (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
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MF59-Seasonal IV (3 to <9 years)	MF59-Seasonal IV (9 to <18 years)	MF59-PANH5N1 IV (6 to <36months)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	16 / 145 (11.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic renal injury			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (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
Blood and lymphatic system disorders			
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (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
Lymphadenitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (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
Volvulus			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (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
Major depression			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (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
Mental disorder			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (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			
Gastroenteritis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	5 / 145 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 145 (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
Respiratory tract infection			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	MF59-PANH5N1 IV (3 to <9 years)	MF59-PANH5N1 IV (9 to <18 years)	MF59-Seasonal IV (6 to <36months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	92 / 96 (95.83%)	92 / 93 (98.92%)	52 / 56 (92.86%)
Nervous system disorders			
Headache			
subjects affected / exposed	34 / 96 (35.42%)	58 / 93 (62.37%)	1 / 56 (1.79%)
occurrences (all)	49	114	1
Somnolence			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	14 / 56 (25.00%)
occurrences (all)	0	0	21
General disorders and administration site conditions			
Chills			
subjects affected / exposed	17 / 96 (17.71%)	18 / 93 (19.35%)	5 / 56 (8.93%)
occurrences (all)	19	33	7
Crying			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	23 / 56 (41.07%)
occurrences (all)	0	0	33
Fatigue			
subjects affected / exposed	38 / 96 (39.58%)	38 / 93 (40.86%)	0 / 56 (0.00%)
occurrences (all)	61	69	0

Injection site erythema			
subjects affected / exposed	58 / 96 (60.42%)	40 / 93 (43.01%)	19 / 56 (33.93%)
occurrences (all)	91	62	27
Injection site haemorrhage			
subjects affected / exposed	14 / 96 (14.58%)	15 / 93 (16.13%)	8 / 56 (14.29%)
occurrences (all)	18	17	8
Injection site induration			
subjects affected / exposed	26 / 96 (27.08%)	32 / 93 (34.41%)	4 / 56 (7.14%)
occurrences (all)	32	48	4
Injection site pain			
subjects affected / exposed	82 / 96 (85.42%)	88 / 93 (94.62%)	22 / 56 (39.29%)
occurrences (all)	163	205	28
Injection site swelling			
subjects affected / exposed	28 / 96 (29.17%)	32 / 93 (34.41%)	4 / 56 (7.14%)
occurrences (all)	33	43	4
Malaise			
subjects affected / exposed	22 / 96 (22.92%)	31 / 93 (33.33%)	0 / 56 (0.00%)
occurrences (all)	31	54	0
Pyrexia			
subjects affected / exposed	17 / 96 (17.71%)	7 / 93 (7.53%)	16 / 56 (28.57%)
occurrences (all)	20	9	20
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 96 (18.75%)	16 / 93 (17.20%)	17 / 56 (30.36%)
occurrences (all)	30	21	23
Nausea			
subjects affected / exposed	16 / 96 (16.67%)	23 / 93 (24.73%)	0 / 56 (0.00%)
occurrences (all)	23	31	0
Teething			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	4 / 56 (7.14%)
occurrences (all)	0	0	6
Vomiting			
subjects affected / exposed	9 / 96 (9.38%)	3 / 93 (3.23%)	6 / 56 (10.71%)
occurrences (all)	10	3	6
Reproductive system and breast disorders			

Dysmenorrhoea			
subjects affected / exposed	0 / 96 (0.00%)	7 / 93 (7.53%)	0 / 56 (0.00%)
occurrences (all)	0	8	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 96 (11.46%)	3 / 93 (3.23%)	7 / 56 (12.50%)
occurrences (all)	12	5	9
Oropharyngeal spasm			
subjects affected / exposed	3 / 96 (3.13%)	7 / 93 (7.53%)	0 / 56 (0.00%)
occurrences (all)	4	7	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	10 / 96 (10.42%)	17 / 93 (18.28%)	1 / 56 (1.79%)
occurrences (all)	13	23	1
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	16 / 56 (28.57%)
occurrences (all)	0	0	20
Irritability			
subjects affected / exposed	0 / 96 (0.00%)	0 / 93 (0.00%)	20 / 56 (35.71%)
occurrences (all)	0	0	30
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 96 (6.25%)	9 / 93 (9.68%)	0 / 56 (0.00%)
occurrences (all)	9	12	0
Myalgia			
subjects affected / exposed	27 / 96 (28.13%)	57 / 93 (61.29%)	0 / 56 (0.00%)
occurrences (all)	36	105	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 96 (1.04%)	0 / 93 (0.00%)	5 / 56 (8.93%)
occurrences (all)	1	0	5
Conjunctivitis			
subjects affected / exposed	6 / 96 (6.25%)	1 / 93 (1.08%)	2 / 56 (3.57%)
occurrences (all)	6	1	3
Ear infection			

subjects affected / exposed	1 / 96 (1.04%)	0 / 93 (0.00%)	2 / 56 (3.57%)
occurrences (all)	1	0	2
Nasopharyngitis			
subjects affected / exposed	3 / 96 (3.13%)	5 / 93 (5.38%)	4 / 56 (7.14%)
occurrences (all)	3	6	4
Otitis media			
subjects affected / exposed	14 / 96 (14.58%)	1 / 93 (1.08%)	14 / 56 (25.00%)
occurrences (all)	22	2	18
Respiratory tract infection			
subjects affected / exposed	3 / 96 (3.13%)	4 / 93 (4.30%)	4 / 56 (7.14%)
occurrences (all)	4	4	5
Rhinitis			
subjects affected / exposed	10 / 96 (10.42%)	6 / 93 (6.45%)	17 / 56 (30.36%)
occurrences (all)	15	6	22
Upper respiratory tract infection			
subjects affected / exposed	8 / 96 (8.33%)	7 / 93 (7.53%)	11 / 56 (19.64%)
occurrences (all)	10	7	13

Non-serious adverse events	MF59-Seasonal IV (3 to <9 years)	MF59-Seasonal IV (9 to <18 years)	MF59-PANH5N1 IV (6 to <36months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 40 (85.00%)	39 / 41 (95.12%)	141 / 145 (97.24%)
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 40 (30.00%)	28 / 41 (68.29%)	2 / 145 (1.38%)
occurrences (all)	20	45	3
Somnolence			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	65 / 145 (44.83%)
occurrences (all)	0	0	99
General disorders and administration site conditions			
Chills			
subjects affected / exposed	9 / 40 (22.50%)	15 / 41 (36.59%)	10 / 145 (6.90%)
occurrences (all)	10	17	12
Crying			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	70 / 145 (48.28%)
occurrences (all)	0	0	142
Fatigue			

subjects affected / exposed	15 / 40 (37.50%)	22 / 41 (53.66%)	0 / 145 (0.00%)
occurrences (all)	24	37	0
Injection site erythema			
subjects affected / exposed	21 / 40 (52.50%)	12 / 41 (29.27%)	90 / 145 (62.07%)
occurrences (all)	26	17	151
Injection site haemorrhage			
subjects affected / exposed	4 / 40 (10.00%)	4 / 41 (9.76%)	28 / 145 (19.31%)
occurrences (all)	6	4	38
Injection site induration			
subjects affected / exposed	6 / 40 (15.00%)	3 / 41 (7.32%)	55 / 145 (37.93%)
occurrences (all)	9	4	71
Injection site pain			
subjects affected / exposed	22 / 40 (55.00%)	35 / 41 (85.37%)	80 / 145 (55.17%)
occurrences (all)	36	56	131
Injection site swelling			
subjects affected / exposed	9 / 40 (22.50%)	11 / 41 (26.83%)	54 / 145 (37.24%)
occurrences (all)	9	14	59
Malaise			
subjects affected / exposed	7 / 40 (17.50%)	17 / 41 (41.46%)	0 / 145 (0.00%)
occurrences (all)	10	22	0
Pyrexia			
subjects affected / exposed	5 / 40 (12.50%)	2 / 41 (4.88%)	60 / 145 (41.38%)
occurrences (all)	5	2	85
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 40 (10.00%)	5 / 41 (12.20%)	55 / 145 (37.93%)
occurrences (all)	4	6	84
Nausea			
subjects affected / exposed	4 / 40 (10.00%)	14 / 41 (34.15%)	0 / 145 (0.00%)
occurrences (all)	5	23	0
Teething			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	2 / 145 (1.38%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	5 / 40 (12.50%)	2 / 41 (4.88%)	20 / 145 (13.79%)
occurrences (all)	6	2	27

Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 145 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 40 (15.00%)	0 / 41 (0.00%)	33 / 145 (22.76%)
occurrences (all)	7	0	54
Oropharyngeal spasm			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	4 / 145 (2.76%)
occurrences (all)	1	0	4
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	5 / 40 (12.50%)	7 / 41 (17.07%)	15 / 145 (10.34%)
occurrences (all)	8	10	18
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	52 / 145 (35.86%)
occurrences (all)	1	0	83
Irritability			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	82 / 145 (56.55%)
occurrences (all)	0	0	154
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 40 (5.00%)	5 / 41 (12.20%)	0 / 145 (0.00%)
occurrences (all)	2	6	0
Myalgia			
subjects affected / exposed	11 / 40 (27.50%)	18 / 41 (43.90%)	0 / 145 (0.00%)
occurrences (all)	13	23	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	11 / 145 (7.59%)
occurrences (all)	1	0	13
Conjunctivitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	12 / 145 (8.28%)
occurrences (all)	1	0	13

Ear infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	20 / 145 (13.79%)
occurrences (all)	0	0	29
Nasopharyngitis			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	15 / 145 (10.34%)
occurrences (all)	0	2	16
Otitis media			
subjects affected / exposed	5 / 40 (12.50%)	0 / 41 (0.00%)	42 / 145 (28.97%)
occurrences (all)	6	0	61
Respiratory tract infection			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	11 / 145 (7.59%)
occurrences (all)	3	0	15
Rhinitis			
subjects affected / exposed	6 / 40 (15.00%)	1 / 41 (2.44%)	41 / 145 (28.28%)
occurrences (all)	6	1	51
Upper respiratory tract infection			
subjects affected / exposed	2 / 40 (5.00%)	2 / 41 (4.88%)	26 / 145 (17.93%)
occurrences (all)	2	2	31

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