Clinical trial results:
A Phase 2, Randomized, Observer-Blind, Multicenter Study to Evaluate the Immunogenicity and Safety of Several Doses of Antigen and MF59 Adjuvant Content in a Monovalent H5N1 Pandemic Influenza Vaccine in Healthy Pediatric Subjects 6 Months to < 9 Years of Age

Summary

EudraCT number	2016-001898-32
Trial protocol	EE Outside EU/EEA
Global end of trial date	15 April 2022

Results information

Result version number	v1 (current)
This version publication date	14 October 2022
First version publication date	14 October 2022

Trial information

Trial identification

Sponsor protocol code	V87_30

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04669691
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Seqirus UK Ltd.
Sponsor organisation address	The Point, 29 Market Street, Maidenhead, United Kingdom, SL6 8AA
Public contact	Clinical Trial Disclosure Manager, Seqirus Inc., Seqirus.ClinicalTrials@seqirus.com
Scientific contact	Clinical Trial Disclosure Manager, Seqirus Inc., Seqirus.ClinicalTrials@seqirus.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001830-PIP01-15, EMEA-000599-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	15 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 April 2022
Global end of trial reached?	Yes
Global end of trial date	15 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Safety Objective:
• To evaluate the safety in each study vaccine group from Day 1 through Day 387, by total population and by age cohort.

Primary Immunogenicity Objective:
• To assess by total population and by age cohort, the antibody responses to each of the study vaccines prior to (Day 1) and at 3 weeks after the first or second vaccination (Day 22 or Day 43), as measured by hemagglutination inhibition (HI) and microneutralization (MN) assays.

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the ICH Harmonized Tripartite Guidelines for GCP, with applicable local regulations, including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, ICH E6 (R2), and Japanese Ministry of Health, Labor, and Welfare, the sponsor codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	19 December 2020
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	Estonia: 100
Country: Number of subjects enrolled	Philippines: 320
Worldwide total number of subjects	420
EEA total number of subjects	100

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)	115
Children (2-11 years)	305
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled from 2 centers in Estonia and 5 centers in the Philippines

Pre-assignment

Screening details:

All enrolled subjects were included in the study

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

1.875 µg H5N1 HA/50% MF59

Arm type	Experimental
Investigational medicinal product name	H5N1 Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The aH5N1 vaccine formulation evaluated in Arm A contained 1.875 µg H5N1 hemagglutinin (HA)/0.125 mL MF59 (=50% MF59)
2 intramuscular injections administered 3 weeks apart (Day 1 and Day 22), in the anterolateral thigh for children <2 years of age and in the deltoid for children ≥2 years of age, unless the deltoid mass was insufficient

Arm title	Arm B

Arm description:

3.75 µg H5N1 HA/50% MF59

Arm type	Experimental
Investigational medicinal product name	H5N1 Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The aH5N1 vaccine formulation evaluated in Arm B contained 3.75 µg H5N1 HA/0.125 mL MF59 (=50% MF59)
2 intramuscular injections administered 3 weeks apart (Day 1 and Day 22), in the anterolateral thigh for children <2 years of age and in the deltoid for children ≥2 years of age, unless the deltoid mass was insufficient

Arm title	Arm C

Arm description:

7.5 µg H5N1 HA/50% MF59

Arm type	Experimental
Investigational medicinal product name	H5N1 Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The aH5N1 vaccine formulation evaluated in Arm C contained 7.5 µg H5N1 HA/0.125 mL MF59 (=50% MF59)
2 intramuscular injections administered 3 weeks apart (Day 1 and Day 22), in the anterolateral thigh for children <2 years of age and in the deltoid for children ≥2 years of age, unless the deltoid mass was insufficient

Arm title	Arm D

Arm description:

1.875 µg H5N1 HA/100% MF59

Arm type	Experimental
Investigational medicinal product name	H5N1 Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The aH5N1 vaccine formulation evaluated in Arm D contained 1.875 µg H5N1 HA/0.25 mL MF59 (=100% MF59)
2 intramuscular injections administered 3 weeks apart (Day 1 and Day 22), in the anterolateral thigh for children <2 years of age and in the deltoid for children ≥2 years of age, unless the deltoid mass was insufficient

Arm title	Arm E

Arm description:

3.75 µg H5N1 HA/100% MF59

Arm type	Experimental
Investigational medicinal product name	H5N1 Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The aH5N1 vaccine formulation evaluated in Arm E contained 3.75 µg H5N1 HA/0.25 mL MF59 (=100% MF59)
2 intramuscular injections administered 3 weeks apart (Day 1 and Day 22), in the anterolateral thigh for children <2 years of age and in the deltoid for children ≥2 years of age, unless the deltoid mass was insufficient

Arm title	Arm F

Arm description:

7.5 µg H5N1 HA/100% MF59

Arm type	Experimental
Investigational medicinal product name	H5N1 Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The aH5N1 vaccine formulation evaluated in Arm F contained 7.5 µg H5N1 HA/0.25 mL MF59 (=100% MF59)
2 intramuscular injections administered 3 weeks apart (Day 1 and Day 22), in the anterolateral thigh for children <2 years of age and in the deltoid for children ≥2 years of age, unless the deltoid mass was insufficient

Number of subjects in period 1	Arm A	Arm B	Arm C
Started	69	72	70
Completed	69	71	70
Not completed	0	1	0
Adverse event, serious fatal	-	1	-

Number of subjects in period 1	Arm D	Arm E	Arm F
Started	70	69	70
Completed	70	69	70
Not completed	0	0	0
Adverse event, serious fatal	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
1.875 µg H5N1 HA/50% MF59	
Reporting group title	Arm B
Reporting group description:	
3.75 µg H5N1 HA/50% MF59	
Reporting group title	Arm C
Reporting group description:	
7.5 µg H5N1 HA/50% MF59	
Reporting group title	Arm D
Reporting group description:	
1.875 µg H5N1 HA/100% MF59	
Reporting group title	Arm E
Reporting group description:	
3.75 µg H5N1 HA/100% MF59	
Reporting group title	Arm F
Reporting group description:	
7.5 µg H5N1 HA/100% MF59	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	69	72	70
Age categorical Units: Subjects			
6 months to <36 months	35	35	35
3 years to <9 years	34	37	35
Age continuous Units: months			
arithmetic mean	48.2	50.9	47.1
standard deviation	± 28.8	± 31.6	± 30.9
Gender categorical Units: Subjects			
Female	31	26	33
Male	38	46	37
Race Units: Subjects			
Asian	52	56	53
Black or African American	0	0	0
White	17	16	17
Ethnicity Units: Subjects			
Not Hispanic or Latino	69	72	70
Received an influenza vaccination in the past 2 years Units: Subjects			
Yes	1	0	3
No	68	72	67

Country Units: Subjects			
Estonia	17	16	17
Philippines	52	56	53
Body mass index Units: kg/m2			
arithmetic mean	16.3	16.3	16.5
standard deviation	± 2.7	± 2.7	± 2.9

Reporting group values	Arm D	Arm E	Arm F
Number of subjects	70	69	70
Age categorical Units: Subjects			
6 months to <36 months	35	36	34
3 years to <9 years	35	33	36
Age continuous Units: months			
arithmetic mean	48.8	49.9	50.6
standard deviation	± 31.8	± 30.8	± 31.8
Gender categorical Units: Subjects			
Female	31	31	40
Male	39	38	30
Race Units: Subjects			
Asian	53	52	53
Black or African American	0	0	1
White	17	17	16
Ethnicity Units: Subjects			
Not Hispanic or Latino	70	69	70
Received an influenza vaccination in the past 2 years Units: Subjects			
Yes	3	3	2
No	67	66	68
Country Units: Subjects			
Estonia	17	17	16
Philippines	53	52	54
Body mass index Units: kg/m2			
arithmetic mean	15.7	15.6	16.1
standard deviation	± 2.0	± 1.9	± 2.6

Reporting group values	Total		
Number of subjects	420		
Age categorical Units: Subjects			
6 months to <36 months	210		
3 years to <9 years	210		

Age continuous Units: months arithmetic mean standard deviation	 -		
Gender categorical Units: Subjects			
Female	192		
Male	228		
Race Units: Subjects			
Asian	319		
Black or African American	1		
White	100		
Ethnicity Units: Subjects			
Not Hispanic or Latino	420		
Received an influenza vaccination in the past 2 years Units: Subjects			
Yes	12		
No	408		
Country Units: Subjects			
Estonia	100		
Philippines	320		
Body mass index Units: kg/m2 arithmetic mean standard deviation	 -		

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description: 1.875 µg H5N1 HA/50% MF59	
Reporting group title	Arm B
Reporting group description: 3.75 µg H5N1 HA/50% MF59	
Reporting group title	Arm C
Reporting group description: 7.5 µg H5N1 HA/50% MF59	
Reporting group title	Arm D
Reporting group description: 1.875 µg H5N1 HA/100% MF59	
Reporting group title	Arm E
Reporting group description: 3.75 µg H5N1 HA/100% MF59	
Reporting group title	Arm F
Reporting group description: 7.5 µg H5N1 HA/100% MF59	
Subject analysis set title	PPS Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description: The PPS Immunogenicity is all subjects in the Full Analysis Set (FAS) immunogenicity who: correctly received the vaccine; provided at least the baseline and one postbaseline blood sample, with evaluable immunogenicity data; had no protocol deviations leading to exclusion as defined prior to unblinding/analysis.	
Subject analysis set title	Solicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the All Exposed Set with any solicited AE data collected, including temperature measurements or use of analgesics/antipyretics.	
Subject analysis set title	Unsolicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the All Exposed Set with unsolicited AE data.	

Primary: Pre- and postvaccination GMTs and GMRs (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Pre- and postvaccination GMTs and GMRs (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)[1]
End point description: Geometric mean titers (GMTs) on Day 1 and Day 22 (3 weeks after the first vaccination) or Day 43 (3 weeks after the second vaccination) as determined by HI assay against the homologous H5N1 pandemic influenza strain. Geometric mean ratios (GMRs) calculated as follows: Day 22/Day 1 or Day 43/Day 1 as determined by HI assay against the homologous H5N1 pandemic influenza strain.	
Subject Analysis Set: PPS Immunogenicity (overall study population)	
End point type	Primary
End point timeframe: Day 1 to 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71	67	66
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.05 (4.8 to 5.3)	5.00 (4.8 to 5.2)	5.21 (5.0 to 5.4)	5.05 (4.8 to 5.3)
GMT Day 22	5.61 (4.9 to 6.4)	6.21 (5.5 to 7.0)	5.98 (5.3 to 6.8)	6.17 (5.4 to 7.0)
GMR Day 22/Day 1	1.11 (1.0 to 1.3)	1.24 (1.1 to 1.4)	1.15 (1.0 to 1.3)	1.22 (1.1 to 1.4)
GMT Day 43	81.10 (58.3 to 112.8)	68.06 (49.4 to 93.8)	86.70 (62.3 to 120.7)	122.43 (87.8 to 170.7)
GMR Day 43/Day 1	16.14 (11.5 to 22.6)	13.77 (9.9 to 19.1)	16.38 (11.7 to 23.0)	24.35 (17.3 to 34.2)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.8 to 5.2)	5.24 (5.0 to 5.5)		
GMT Day 22	6.47 (5.7 to 7.3)	5.78 (5.1 to 6.6)		
GMR Day 22/Day 1	1.29 (1.1 to 1.5)	1.11 (1.0 to 1.3)		
GMT Day 43	123.37 (89.1 to 170.8)	123.61 (88.8 to 172.1)		
GMR Day 43/Day 1	24.98 (17.9 to 34.8)	23.14 (16.5 to 32.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Pre- and postvaccination GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point title	Pre- and postvaccination GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)[2]

End point description:

GMTs on Day 1 and Day 22 (3 weeks after the first vaccination) or Day 43 (3 weeks after the second

vaccination) as determined by HI assay against the homologous H5N1 pandemic influenza strain. GMRs calculated as follows: Day 22/Day 1 or Day 43/Day 1 as determined by HI assay against the homologous H5N1 pandemic influenza strain.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Primary

End point timeframe:

Day 1 to Day 43

Notes:

[2] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.10 (4.9 to 5.3)	5.00 (4.8 to 5.2)	5.42 (5.2 to 5.7)	5.11 (4.9 to 5.3)
GMT Day 22	5.59 (4.7 to 6.6)	6.14 (5.2 to 7.3)	5.51 (4.6 to 6.6)	6.23 (5.2 to 7.4)
GMR Day 22/Day 1	1.10 (0.9 to 1.3)	1.21 (1.0 to 1.4)	1.05 (0.9 to 1.3)	1.22 (1.0 to 1.5)
GMT Day 43	93.22 (56.5 to 153.7)	98.37 (59.6 to 162.4)	102.28 (61.5 to 170.1)	129.72 (78.1 to 215.5)
GMR Day 43/Day 1	18.27 (11.1 to 30.1)	19.62 (11.9 to 32.4)	19.02 (11.5 to 31.4)	25.41 (15.3 to 42.2)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	31		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.8 to 5.2)	5.00 (4.8 to 5.2)		
GMT Day 22	6.55 (5.5 to 7.8)	5.78 (4.8 to 6.9)		
GMR Day 22/Day 1	1.30 (1.1 to 1.5)	1.14 (1.0 to 1.4)		
GMT Day 43	157.44 (96.7 to 256.3)	120.07 (71.0 to 202.9)		
GMR Day 43/Day 1	31.39 (19.3 to 51.1)	23.94 (14.2 to 40.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Pre- and postvaccination GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point title	Pre- and postvaccination GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)[3]

End point description:

GMTs on Day 1 and Day 22 (3 weeks after the first vaccination) or Day 43 (3 weeks after the second vaccination) as determined by HI assay against the homologous H5N1 pandemic influenza strain.
GMRs calculated as follows: Day 22/Day 1 or Day 43/Day 1 as determined by HI assay against the homologous H5N1 pandemic influenza strain.

Subject Analysis Set: PPS Immunogenicity (3 years to <9 years age cohort)

End point type	Primary

End point timeframe:

Day 1 to 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	33	33
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.6 to 5.4)	5.00 (4.7 to 5.4)	5.00 (4.6 to 5.4)	5.00 (4.6 to 5.4)
GMT Day 22	5.61 (4.6 to 6.8)	6.32 (5.3 to 7.6)	6.29 (5.2 to 7.6)	6.10 (5.0 to 7.4)
GMR Day 22/Day 1	1.12 (0.9 to 1.4)	1.26 (1.0 to 1.5)	1.26 (1.0 to 1.5)	1.22 (1.0 to 1.5)
GMT Day 43	70.21 (45.5 to 108.4)	48.35 (32.1 to 72.9)	69.40 (44.9 to 107.2)	114.85 (74.4 to 177.4)
GMR Day 43/Day 1	14.27 (9.0 to 22.6)	9.83 (6.4 to 15.2)	14.10 (8.9 to 22.3)	23.34 (14.7 to 37.0)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.6 to 5.4)	5.45 (5.1 to 5.9)		
GMT Day 22	6.42 (5.3 to 7.8)	5.91 (4.9 to 7.1)		
GMR Day 22/Day 1	1.29 (1.0 to 1.6)	1.08 (0.9 to 1.3)		
GMT Day 43	97.17 (62.9 to 150.1)	129.15 (84.9 to 196.6)		
GMR Day 43/Day 1	19.75 (12.5 to 31.3)	21.98 (14.2 to 34.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)[4]

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 22 or 43.
Percentage of subjects achieving seroconversion with a titer ≥1:40 on Days 1, 22 or 43.

Subject Analysis Set: PPS Immunogenicity (overall study population)

End point type	Primary

End point timeframe:

Day 1 to Day 43

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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71	67	66
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	0.0 (0.00 to 5.36)	4.2 (0.88 to 11.86)	3.0 (0.36 to 10.37)	4.5 (0.95 to 12.71)
% of subjects with seroconversion at Day 43	82.1 (70.80 to 90.39)	74.6 (62.92 to 84.23)	77.6 (65.78 to 86.89)	90.9 (81.26 to 96.59)
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.06)	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.44)
% of subjects with HI titer ≥1:40 at Day 22	0.0 (0.00 to 5.36)	4.2 (0.88 to 11.86)	3.0 (0.36 to 10.37)	4.5 (0.95 to 12.71)
% of subjects with HI titer ≥1:40 at Day 43	82.1 (70.80 to 90.39)	74.6 (62.92 to 84.23)	77.6 (65.78 to 86.89)	90.9 (81.26 to 96.59)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67		
Units: Percentage of subjects				
number (confidence interval 95%)				

% of subjects with seroconversion at Day 22	1.4 (0.04 to 7.81)	3.0 (0.36 to 10.37)		
% of subjects with seroconversion at Day 43	87.0 (76.68 to 93.86)	86.6 (76.03 to 93.67)		
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 5.21)	1.5 (0.04 to 8.04)		
% of subjects with HI titer ≥1:40 at Day 22	1.4 (0.04 to 7.81)	3.0 (0.36 to 10.37)		
% of subjects with HI titer ≥1:40 at Day 43	87.0 (76.68 to 93.86)	86.6 (76.03 to 93.67)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point title	Percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)[5]

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 22 or 43.
Percentage of subjects achieving seroconversion with a titer ≥1:40 on Days 1, 22 or 43.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Primary

End point timeframe:

Day 1 to 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	0.0 (0.00 to 10.28)	2.9 (0.07 to 15.33)	0.0 (0.00 to 10.28)	3.0 (0.08 to 15.76)
% of subjects with seroconversion at Day 43	79.4 (62.10 to 91.30)	82.4 (65.47 to 93.24)	79.4 (62.10 to 91.30)	93.9 (79.77 to 99.26)
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.58)
% of subjects with HI titer ≥1:40 at Day 22	0.0 (0.00 to 10.28)	2.9 (0.07 to 15.33)	0.0 (0.00 to 10.28)	3.0 (0.08 to 15.76)
% of subjects with HI titer ≥1:40 at Day 43	79.4 (62.10 to 91.30)	82.4 (65.47 to 93.24)	79.4 (62.10 to 91.30)	93.9 (79.77 to 99.26)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	31		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	0.0 (0.00 to 9.74)	3.2 (0.08 to 16.70)		
% of subjects with seroconversion at Day 43	86.1 (70.50 to 95.33)	87.1 (70.17 to 96.37)		
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 9.74)	0.0 (0.00 to 11.22)		
% of subjects with HI titer ≥1:40 at Day 22	0.0 (0.00 to 9.74)	3.2 (0.08 to 16.70)		
% of subjects with HI titer ≥1:40 at Day 43	86.1 (70.50 to 95.33)	87.1 (70.17 to 96.37)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point title	Percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)[6]

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 22 or 43.
Percentage of subjects achieving seroconversion with a titer ≥1:40 on Days 1, 22 or 43.

Subject Analysis Set: PPS Immunogenicity (3 years to <9 years age cohort)

End point type	Primary

End point timeframe:

Day 1 to Day 43

Notes:

[6] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	33	33
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	0.0 (0.00 to 10.58)	5.4 (0.66 to 18.19)	6.1 (0.74 to 20.23)	6.1 (0.74 to 20.23)
% of subjects with seroconversion at Day 43	84.8 (68.10 to 94.89)	67.6 (50.21 to 81.99)	75.8 (57.74 to 88.91)	87.9 (71.80 to 96.60)
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	0.0 (0.00 to 9.49)	0.0 (0.00 to 10.58)	0.0 (0.00 to 10.58)
% of subjects with HI titer ≥1:40 at Day 22	0.0 (0.00 to 10.58)	5.4 (0.66 to 18.19)	6.1 (0.74 to 20.23)	6.1 (0.74 to 20.23)

% of subjects with HI titer ≥1:40 at Day 43	84.8 (68.10 to 94.89)	67.6 (50.21 to 81.99)	75.8 (57.74 to 88.91)	87.9 (71.80 to 96.60)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	3.0 (0.08 to 15.76)	2.8 (0.07 to 14.53)		
% of subjects with seroconversion at Day 43	87.9 (71.80 to 96.60)	86.1 (70.50 to 95.33)		
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	2.8 (0.07 to 14.53)		
% of subjects with HI titer ≥1:40 at Day 22	3.0 (0.08 to 15.76)	2.8 (0.07 to 14.53)		
% of subjects with HI titer ≥1:40 at Day 43	87.9 (71.80 to 96.60)	86.1 (70.50 to 95.33)		

Statistical analyses

No statistical analyses for this end point

Primary: Pre- and postvaccination GMTs and GMRs (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Pre- and postvaccination GMTs and GMRs (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)[7]

End point description:

GMTs on Day 1 and Day 22 (3 weeks after the first vaccination) or Day 43 (3 weeks after the second vaccination) as determined by MN assay against the homologous H5N1 pandemic influenza strain. GMRs calculated as follows: Day 22/Day 1 or Day 43/Day 1 as determined by MN assay against the homologous H5N1 pandemic influenza strain.

Subject Analysis Set: PPS Immunogenicity (overall study population)

End point type	Primary

End point timeframe:

Day 1 to 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71[8]	67	66[9]
Units: Titer / ratio				
geometric mean (confidence interval 95%)				

GMT Day 1	5.19 (4.9 to 5.5)	5.27 (5.0 to 5.6)	5.38 (5.1 to 5.7)	5.16 (4.9 to 5.5)
GMT Day 22	31.42 (24.7 to 40.0)	34.83 (27.5 to 44.2)	40.61 (31.9 to 51.7)	46.08 (36.0 to 59.0)
GMR Day 22/Day 1	6.02 (4.7 to 7.7)	6.62 (5.2 to 8.4)	7.66 (6.0 to 9.8)	8.85 (6.9 to 11.3)
GMT Day 43	531.04 (424.7 to 664.1)	667.86 (536.7 to 831.1)	610.37 (488.0 to 763.4)	619.44 (494.5 to 775.9)
GMR Day 43/Day 1	102.26 (81.4 to 128.5)	126.71 (101.4 to 158.4)	113.98 (90.7 to 143.2)	119.78 (95.2 to 150.7)

Notes:

[8] - n=69 at Day 22; n=70 at Day 43

[9] - n=64 at Day 22

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69[10]	67		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.13 (4.9 to 5.4)	5.31 (5.0 to 5.6)		
GMT Day 22	54.66 (42.9 to 69.7)	52.81 (41.5 to 67.2)		
GMR Day 22/Day 1	10.52 (8.2 to 13.4)	10.02 (7.9 to 12.8)		
GMT Day 43	864.91 (693.8 to 1078.2)	766.18 (612.6 to 958.2)		
GMR Day 43/Day 1	168.06 (134.2 to 210.5)	144.55 (115.0 to 181.6)		

Notes:

[10] - n=66 at Day 22

Statistical analyses

No statistical analyses for this end point

Primary: Pre- and postvaccination GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point title	Pre- and postvaccination GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)[11]

End point description:

GMTs on Day 1 and Day 22 (3 weeks after the first vaccination) or Day 43 (3 weeks after the second vaccination) as determined by MN assay against the homologous H5N1 pandemic influenza strain. GMRs calculated as follows: Day 22/Day 1 or Day 43/Day 1 as determined by MN assay against the homologous H5N1 pandemic influenza strain.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Primary

End point timeframe:

Day 1 to 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33[12]
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.7 to 5.3)	5.00 (4.7 to 5.3)	5.26 (4.9 to 5.6)	5.21 (4.9 to 5.6)
GMT Day 22	29.27 (21.0 to 40.8)	33.14 (23.8 to 46.2)	24.93 (17.9 to 34.7)	45.78 (32.3 to 64.8)
GMR Day 22/Day 1	5.76 (4.1 to 8.0)	6.52 (4.7 to 9.1)	4.80 (3.4 to 6.7)	8.84 (6.2 to 12.5)
GMT Day 43	618.77 (448.2 to 854.3)	910.32 (659.3 to 1256.9)	717.83 (520.0 to 991.0)	725.06 (522.8 to 1005.5)
GMR Day 43/Day 1	122.81 (88.8 to 169.9)	180.68 (130.6 to 250.0)	137.36 (99.3 to 190.0)	139.62 (100.4 to 194.1)

Notes:

[12] - n=31 at Day 22

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[13]	31		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.10 (4.8 to 5.4)	5.29 (4.9 to 5.7)		
GMT Day 22	69.41 (49.8 to 96.7)	42.07 (29.7 to 59.6)		
GMR Day 22/Day 1	13.54 (9.7 to 18.9)	8.09 (5.7 to 11.4)		
GMT Day 43	1094.07 (800.0 to 1496.2)	863.94 (616.3 to 1211.2)		
GMR Day 43/Day 1	214.16 (156.2 to 293.6)	164.74 (117.3 to 231.4)		

Notes:

[13] - n=34 at Day 22

Statistical analyses

No statistical analyses for this end point

Primary: Pre- and postvaccination GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 3 years to 9 years age cohort (PPS Immunogenicity)

End point title	Pre- and postvaccination GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 3 years to 9 years age cohort (PPS Immunogenicity)[14]

End point description:

GMTs on Day 1 and Day 22 (3 weeks after the first vaccination) or Day 43 (3 weeks after the second vaccination) as determined by MN assay against the homologous H5N1 pandemic influenza strain. GMRs calculated as follows: Day 22/Day 1 or Day 43/Day 1 as determined by MN assay against the homologous H5N1 pandemic influenza strain.

Subject Analysis Set: PPS Immunogenicity (3 years to 9 years age cohort)

End point type	Primary

End point timeframe:

Day 1 to Day 43

Notes:

[14] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37[15]	33	33
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.38 (4.9 to 5.9)	5.54 (5.1 to 6.0)	5.49 (5.0 to 6.0)	5.11 (4.7 to 5.6)
GMT Day 22	33.70 (24.0 to 47.4)	36.69 (26.3 to 51.1)	66.97 (47.6 to 94.2)	46.59 (33.1 to 65.6)
GMR Day 22/Day 1	6.29 (4.5 to 8.9)	6.73 (4.8 to 9.4)	12.37 (8.8 to 17.4)	8.90 (6.3 to 12.5)
GMT Day 43	458.11 (334.2 to 627.9)	495.77 (366.4 to 670.9)	518.46 (378.2 to 710.8)	527.09 (384.3 to 723.0)
GMR Day 43/Day 1	85.22 (61.6 to 118.0)	89.57 (65.6 to 122.3)	94.64 (68.4 to 131.0)	102.76 (74.2 to 142.3)

Notes:

[15] - n=35 at Day 22; n=36 at Day 43

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33[16]	36		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.16 (4.7 to 5.7)	5.35 (4.9 to 5.8)		
GMT Day 22	42.11 (29.8 to 59.6)	65.11 (47.0 to 90.2)		
GMR Day 22/Day 1	8.00 (5.7 to 11.3)	12.18 (8.8 to 16.9)		
GMT Day 43	680.71 (496.4 to 933.4)	670.67 (495.9 to 907.0)		
GMR Day 43/Day 1	131.50 (95.0 to 182.0)	125.44 (91.9 to 171.3)		

Notes:

[16] - n=32 at Day 22

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Percentage of subjects with seroconversion and percentage of

	subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)[17]

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 22 or 43.
Percentage of subjects achieving seroconversion with a titer ≥1:40 on Days 1, 22 or 43.

Subject Analysis Set: PPS Immunogenicity (overall study population)

End point type	Primary

End point timeframe:

Day 1 to 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71[18]	67	66[19]
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	44.8 (32.60 to 57.42)	56.5 (44.04 to 68.42)	58.2 (45.52 to 70.15)	67.2 (54.31 to 78.41)
% of subjects with seroconversion at Day 43	100.0 (94.64 to 100.00)	100.0 (94.87 to 100.00)	100.0 (94.64 to 100.00)	100.0 (94.56 to 100.00)
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.06)	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.44)
% of subjects with MN titer ≥1:40 at Day 22	44.8 (32.60 to 57.42)	56.5 (44.04 to 68.42)	58.2 (45.52 to 70.15)	67.2 (54.31 to 78.41)
% of subjects with MN titer ≥1:40 at Day 43	100.0 (94.64 to 100.00)	100.0 (94.87 to 100.00)	100.0 (94.64 to 100.00)	100.0 (94.56 to 100.00)

Notes:

[18] - n=69 at Day 22; n=70 at Day 43

[19] - n=64 at Day 22

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69[20]	67		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	72.7 (60.36 to 82.97)	68.7 (56.16 to 79.44)		
% of subjects with seroconversion at Day 43	100.0 (94.79 to 100.00)	100.0 (94.64 to 100.00)		
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 5.21)	0.0 (0.00 to 5.36)		
% of subjects with MN titer ≥1:40 at Day 22	72.7 (60.36 to 82.97)	68.7 (56.16 to 79.44)		
% of subjects with MN titer ≥1:40 at Day 43	100.0 (94.79 to 100.00)	100.0 (94.64 to 100.00)		

Notes:

[20] - n=66 at Day 22

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point title	Percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)[21]

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 22 or 43.
Percentage of subjects achieving seroconversion with a titer ≥1:40 on Days 1, 22 or 43.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Primary

End point timeframe:

Day 1 to Day 43

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33[22]
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	35.3 (19.75 to 53.51)	55.9 (37.89 to 72.81)	35.3 (19.75 to 53.51)	71.0 (51.96 to 85.78)
% of subjects with seroconversion at Day 43	100.0 (89.72 to 100.00)	100.0 (89.72 to 100.00)	100.0 (89.72 to 100.00)	100.0 (89.42 to 100.00)
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.58)
% of subjects with MN titer ≥1:40 at Day 22	35.3 (19.75 to 53.51)	55.9 (37.89 to 72.81)	35.3 (19.75 to 53.51)	71.0 (51.96 to 85.78)
% of subjects with MN titer ≥1:40 at Day 43	100.0 (89.72 to 100.00)	100.0 (89.72 to 100.00)	100.0 (89.72 to 100.00)	100.0 (89.42 to 100.00)

Notes:

[22] - n=31 at Day 22

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[23]	31		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	82.4 (65.47 to 93.24)	58.1 (39.08 to 75.45)		
% of subjects with seroconversion at Day 43	100.0 (90.26 to 100.00)	100.0 (88.78 to 100.00)		
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 9.74)	0.0 (0.00 to 11.22)		
% of subjects with MN titer ≥1:40 at Day 22	82.4 (65.47 to 93.24)	58.1 (39.08 to 75.45)		

% of subjects with MN titer ≥1:40 at Day 43	100.0 (90.26 to 100.00)	100.0 (88.78 to 100.00)		

Notes:

[23] - n=34 at Day 22

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point title	Percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)[24]

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 22 or 43.
Percentage of subjects achieving seroconversion with a titer ≥1:40 on Days 1, 22 or 43.

Subject Analysis Set: PPS Immunogenicity (3 years to < 9 years age cohort)

End point type	Primary

End point timeframe:

Day 1 to Day 43

Notes:

[24] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37[25]	33	33
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 22	54.5 (36.35 to 71.89)	57.1 (39.35 to 73.68)	81.8 (64.54 to 93.02)	63.6 (45.12 to 79.60)
% of subjects with seroconversion at Day 43	100.0 (89.42 to 100.00)	100.0 (90.26 to 100.00)	100.0 (89.42 to 100.00)	100.0 (89.42 to 100.00)
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	0.0 (0.00 to 9.49)	0.0 (0.00 to 10.58)	0.0 (0.00 to 10.58)
% of subjects with MN titer ≥1:40 at Day 22	54.5 (36.35 to 71.89)	57.1 (39.35 to 73.68)	81.8 (64.54 to 93.02)	63.6 (45.12 to 79.60)
% of subjects with MN titer ≥1:40 at Day 43	100.0 (89.42 to 100.00)	100.0 (90.26 to 100.00)	100.0 (89.42 to 100.00)	100.0 (89.42 to 100.00)

Notes:

[25] - n=35 at Day 22; n=36 at Day 43

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33[26]	36		
Units: Percentage of subjects				
number (confidence interval 95%)				

% of subjects with seroconversion at Day 22	62.5 (43.69 to 78.90)	77.8 (60.85 to 89.88)		
% of subjects with seroconversion at Day 43	100.0 (89.42 to 100.00)	100.0 (90.26 to 100.00)		
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	0.0 (0.00 to 9.74)		
% of subjects with MN titer ≥1:40 at Day 22	62.5 (43.69 to 78.90)	77.8 (60.85 to 89.88)		
% of subjects with MN titer ≥1:40 at Day 43	100.0 (89.42 to 100.00)	100.0 (90.26 to 100.00)		

Notes:

[26] - n=32 at Day 22

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with solicited adverse events (AEs) from Day 1 through Day 7 after any vaccination in the overall study population (Solicited Safety Set)

End point title	Percentages of subjects with solicited adverse events (AEs) from Day 1 through Day 7 after any vaccination in the overall study population (Solicited Safety Set)[27]

End point description:

Percentages of subjects with solicited local and systemic AEs that occurred within 7 days following each vaccination.

Subject Analysis Set: Solicited Safety Set (overall study population)

End point type	Primary

End point timeframe:

Day 1 through Day 7 after any vaccination

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	72	70	70
Units: Percentage of subjects				
number (not applicable)				
Any solicited AE	46.4	45.8	45.7	48.6
Solicited local AEs	27.5	22.2	22.9	30.0
Solicited systemic AEs	30.4	33.3	28.6	34.3
Analgesic/antipyretic use	13.0	9.7	8.6	7.1

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	70		
Units: Percentage of subjects				
number (not applicable)				

Any solicited AE	53.6	44.3		
Solicited local AEs	27.5	24.3		
Solicited systemic AEs	42.0	25.7		
Analgesic/antipyretic use	7.2	12.9		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with solicited adverse events (AEs) from Day 1 through Day 7 after any vaccination in the 6 months to <36 months age cohort (Solicited Safety Set)

End point title	Percentages of subjects with solicited adverse events (AEs) from Day 1 through Day 7 after any vaccination in the 6 months to <36 months age cohort (Solicited Safety Set)[28]

End point description:

Percentages of subjects with solicited local and systemic AEs that occurred within 7 days following each vaccination.

Subject Analysis Set: Solicited Safety Set (6 months to <36 months age cohort)

End point type	Primary

End point timeframe:

Day 1 through Day 7 after any vaccination

Notes:

[28] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	35	35	35
Units: Percentage of subjects				
number (not applicable)				
Any solicited AE	42.9	57.1	51.4	57.1
Solicited local AEs	20.0	28.6	17.1	31.4
Solicited systemic AEs	40.0	42.9	45.7	45.7
Analgesic/antipyretic use	14.3	11.4	11.4	8.6

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage of subjects				
number (not applicable)				
Any solicited AE	58.3	44.1		
Solicited local AEs	22.2	11.8		
Solicited systemic AEs	50.0	32.4		
Analgesic/antipyretic use	8.3	17.6		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with solicited adverse events (AEs) from Day 1 through Day 7 after any vaccination in the 3 years to <9 years age cohort (Solicited Safety Set)

End point title	Percentages of subjects with solicited adverse events (AEs) from Day 1 through Day 7 after any vaccination in the 3 years to <9 years age cohort (Solicited Safety Set)[29]

End point description:

Percentages of subjects with solicited local and systemic AEs that occurred within 7 days following each vaccination.

Subject Analysis Set: Solicited Safety Set (3 years to <9 years age cohort)

End point type	Primary

End point timeframe:

Day 1 through Day 7 after any vaccination

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	37	35	35
Units: Percentage of subjects				
number (not applicable)				
Any solicited AE	50.0	35.1	40.0	40.0
Solicited local AEs	35.3	16.2	28.6	28.6
Solicited systemic AEs	20.6	24.3	11.4	22.9
Analgesic/antipyretic use	11.8	8.1	5.7	5.7

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: Percentage of subjects				
number (not applicable)				
Any solicited AE	48.5	44.4		
Solicited local AEs	33.3	36.1		
Solicited systemic AEs	33.3	19.4		
Analgesic/antipyretic use	6.1	8.3		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination in the overall study population (Unsolicited Safety Set)

End point title	Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination in the overall study population (Unsolicited Safety Set)[30]

End point description:

Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination within each vaccine group.

Subject Analysis Set: Unsolicited Safety Set (overall study population)

End point type	Primary

End point timeframe:

Within 21 days after any vaccination

Notes:

[30] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	72	70	70
Units: Percentage of subjects				
number (not applicable)				
Unsolicited AEs, Any	26.1	20.8	28.6	14.3
Unsolicited AEs, Mild	26.1	19.4	28.6	14.3
Unsolicited AEs, Moderate	0	1.4	0	0
Unsolicited AEs, Severe	0	0	0	0
Unsolicited AEs, Related	2.9	2.8	2.9	0

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	70		
Units: Percentage of subjects				
number (not applicable)				
Unsolicited AEs, Any	21.7	17.1		
Unsolicited AEs, Mild	17.4	12.9		
Unsolicited AEs, Moderate	4.3	2.9		
Unsolicited AEs, Severe	0	1.4		
Unsolicited AEs, Related	2.9	1.4		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination in the 6 months to <36 months age cohort (Unsolicited Safety Set)

End point title	Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination in the 6 months to <36 months age cohort (Unsolicited Safety Set)[31]

End point description:

Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination within each vaccine group.

Subject Analysis Set: Unsolicited Safety Set (6 months to <36 months age cohort)

End point type	Primary

End point timeframe:

Within 21 days after any vaccination

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	35	35	35
Units: Percentage of subjects				
number (not applicable)				
Unsolicited AEs, Any	34.3	31.4	37.1	22.9
Unsolicited AEs, Mild	34.3	28.6	37.1	22.9
Unsolicited AEs, Moderate	0	2.9	0	0
Unsolicited AEs, Severe	0	0	0	0
Unsolicited AEs, Related	2.9	5.7	5.7	0

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage of subjects				
number (not applicable)				
Unsolicited AEs, Any	22.2	20.6		
Unsolicited AEs, Mild	19.4	14.7		
Unsolicited AEs, Moderate	2.8	5.9		
Unsolicited AEs, Severe	0	0		

Unsolicited AEs, Related	2.8	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination in the 3 years to <9 years age cohort (Unsolicited Safety Set)

End point title	Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination in the 3 years to <9 years age cohort (Unsolicited Safety Set)[32]

End point description:

Percentages of subjects with any unsolicited AEs reported within 21 days after each vaccination within each vaccine group.

Subject Analysis Set: Unsolicited Safety Set (3 years to <9 years age cohort)

End point type	Primary

End point timeframe:

Within 21 days after any vaccination

Notes:

[32] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	37	35	35
Units: Percentage of subjects				
number (not applicable)				
Unsolicited AEs, Any	17.6	10.8	20.0	5.7
Unsolicited AEs, Mild	17.6	10.8	20.0	5.7
Unsolicited AEs, Moderate	0	0	0	0
Unsolicited AEs, Severe	0	0	0	0
Unsolicited AEs, Related	2.9	0	0	0

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: Percentage of subjects				
number (not applicable)				
Unsolicited AEs, Any	21.2	13.9		
Unsolicited AEs, Mild	15.2	11.1		
Unsolicited AEs, Moderate	6.1	0		
Unsolicited AEs, Severe	0	2.8		
Unsolicited AEs, Related	3.0	2.8		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects reporting serious adverse events (SAEs), new onset of chronic disease (NOCD), adverse events of special interest (AESIs), and AEs leading to vaccine and/or study withdrawal in the overall study population (Unsolicited Safety Set)

End point title	Percentages of subjects reporting serious adverse events (SAEs), new onset of chronic disease (NOCD), adverse events of special interest (AESIs), and AEs leading to vaccine and/or study withdrawal in the overall study population (Unsolicited Safety Set)[33]

End point description:

Percentages of subjects reporting SAEs, NOCD, AESIs, and AEs leading to vaccine and/or study withdrawal, as collected from Day 1 through Day 387.

Subject Analysis Set: Unsolicited Safety Set (overall study population)

End point type	Primary

End point timeframe:

Day 1 through Day 387

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	72	70	70
Units: Percentage of subjects				
number (not applicable)				
SAE	0	1.4	4.3	0
Related SAE	0	0	0	0
NOCD	0	1.4	0	0
AESI	0	0	0	0
AE leading to withdrawal	0	0	0	0
Death	0	1.4	0	0

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	70		
Units: Percentage of subjects				
number (not applicable)				
SAE	1.4	4.3		

Related SAE	0	0		
NOCD	0	0		
AESI	0	0		
AE leading to withdrawal	0	0		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects reporting SAEs, NOCD, AESIs, and AEs leading to vaccine and/or study withdrawal in the 6 months to <36 months age (Unsolicited Safety Set)

End point title	Percentages of subjects reporting SAEs, NOCD, AESIs, and AEs leading to vaccine and/or study withdrawal in the 6 months to <36 months age (Unsolicited Safety Set)[34]

End point description:

Percentages of subjects reporting SAEs, NOCD, AESIs, and AEs leading to vaccine and/or study withdrawal, as collected from Day 1 through Day 387.

Subject Analysis Set: Unsolicited Safety Set (6 months to <36 months age cohort)

End point type	Primary

End point timeframe:

Day 1 through Day 387

Notes:

[34] - 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: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	35	35	35
Units: Percentage of subjects				
number (not applicable)				
SAE	0	2.9	2.9	0
Related SAE	0	0	0	0
NOCD	0	0	0	0
AESI	0	0	0	0
AE leading to withdrawal	0	0	0	0
Death	0	2.9	0	0

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Percentage of subjects				
number (not applicable)				
SAE	2.8	5.9		
Related SAE	0	0		

NOCD	0	0		
AESI	0	0		
AE leading to withdrawal	0	0		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of subjects reporting SAEs, NOCD, AESIs, and AEs leading to vaccine and/or study withdrawal in the 3 years to <9 years age (Unsolicited Safety Set)

End point title	Percentages of subjects reporting SAEs, NOCD, AESIs, and AEs leading to vaccine and/or study withdrawal in the 3 years to <9 years age (Unsolicited Safety Set)[35]

End point description:

Percentages of subjects reporting SAEs, NOCD, AESIs, and AEs leading to vaccine and/or study withdrawal, as collected from Day 1 through Day 387.

Subject Analysis Set: Unsolicited Safety Set (3 years to <9 years age cohort)

End point type	Primary

End point timeframe:

Day 1 through Day 387

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was mainly descriptive in nature without any prespecified inferential analyses.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	37	35	35
Units: Percentage of subjects				
number (not applicable)				
SAE	0	0	5.7	0
Related SAE	0	0	0	0
NOCD	0	2.7	0	0
AESI	0	0	0	0
AE leading to withdrawal	0	0	0	0
Death	0	0	0	0

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: Percentage of subjects				
number (not applicable)				
SAE	0	2.8		
Related SAE	0	0		
NOCD	0	0		

AESI	0	0		
AE leading to withdrawal	0	0		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - GMTs and GMRs (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - GMTs and GMRs (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point description:

GMTs on Day 1 and Day 202 (6 months after the second vaccination) as determined by HI assay.
GMRs calculated as follows: Day 202/Day 1 as determined by HI assay.

Subject Analysis Set: PPS Immunogenicity (overall study population)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71	67	66
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.05 (4.8 to 5.3)	5.00 (4.8 to 5.2)	5.21 (5.0 to 5.4)	5.05 (4.8 to 5.3)
GMT Day 202	7.92 (6.3 to 9.9)	8.90 (7.2 to 11.0)	8.81 (7.1 to 11.0)	10.19 (8.2 to 12.7)
GMR Day 202/Day 1	1.57 (1.3 to 2.0)	1.78 (1.4 to 2.2)	1.69 (1.3 to 2.1)	2.02 (1.6 to 2.5)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.8 to 5.2)	5.24 (5.0 to 5.5)		
GMT Day 202	12.90 (10.4 to 16.1)	13.15 (10.5 to 16.4)		

GMR Day 202/Day 1	2.59 (2.1 to 3.2)	2.50 (2.0 to 3.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point description:

GMTs on Day 1 and Day 202 (6 months after the second vaccination) as determined by HI assay.
GMRs calculated as follows: Day 202/Day 1 as determined by HI assay.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.10 (4.9 to 5.3)	5.00 (4.8 to 5.2)	5.42 (5.2 to 5.7)	5.11 (4.9 to 5.3)
GMT Day 202	9.11 (6.3 to 13.3)	12.57 (8.6 to 18.3)	11.60 (7.9 to 17.0)	13.55 (9.3 to 19.8)
GMR Day 202/Day 1	1.79 (1.2 to 2.6)	2.50 (1.7 to 3.6)	2.17 (1.5 to 3.2)	2.65 (1.8 to 3.9)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	31		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.8 to 5.2)	5.00 (4.8 to 5.2)		
GMT Day 202	19.12 (13.3 to 27.6)	19.00 (12.8 to 28.2)		

GMR Day 202/Day 1	3.81 (2.6 to 5.5)	3.78 (2.5 to 5.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - GMTs and GMRs (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point description:

GMTs on Day 1 and Day 202 (6 months after the second vaccination) as determined by HI assay.
GMRs calculated as follows: Day 202/Day 1 as determined by HI assay.

Subject Analysis Set: PPS Immunogenicity (3 years to <9 years age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	33	33
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.6 to 5.4)	5.00 (4.7 to 5.4)	5.00 (4.6 to 5.4)	5.00 (4.6 to 5.4)
GMT Day 202	6.90 (5.4 to 8.8)	6.36 (5.1 to 8.0)	6.55 (5.2 to 8.3)	7.66 (6.0 to 9.7)
GMR Day 202/Day 1	1.38 (1.1 to 1.8)	1.28 (1.0 to 1.6)	1.31 (1.0 to 1.7)	1.54 (1.2 to 2.0)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.6 to 5.4)	5.45 (5.1 to 5.9)		
GMT Day 202	8.69 (6.8 to 11.0)	9.30 (7.4 to 11.7)		

GMR Day 202/Day 1	1.74 (1.4 to 2.2)	1.68 (1.3 to 2.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 202.
Percentage of subjects achieving seroconversion with a titer of ≥1:40 on Day 202.

Subject Analysis Set: PPS Immunogenicity (overall study population)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71	67	66
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	10.4 (4.30 to 20.35)	14.1 (6.97 to 24.38)	11.9 (5.30 to 22.18)	15.2 (7.51 to 26.10)
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.06)	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.44)
% of subjects with HI titer ≥1:40 at Day 202	10.4 (4.30 to 20.35)	14.1 (6.97 to 24.38)	11.9 (5.30 to 22.18)	15.2 (7.51 to 26.10)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	21.7 (12.71 to 33.31)	25.4 (15.53 to 37.49)		
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 5.21)	1.5 (0.04 to 8.04)		

% of subjects with HI titer ≥1:40 at Day 202	21.7 (12.71 to 33.31)	25.4 (15.53 to 37.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 202.
Percentage of subjects achieving seroconversion with a titer of ≥1:40 on Day 202.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	17.6 (6.76 to 34.53)	26.5 (12.88 to 44.36)	23.5 (10.75 to 41.17)	27.3 (13.30 to 45.52)
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.58)
% of subjects with HI titer ≥1:40 at Day 202	17.6 (6.76 to 34.53)	26.5 (12.88 to 44.36)	23.5 (10.75 to 41.17)	27.3 (13.30 to 45.52)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	31		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	33.3 (18.56 to 50.97)	41.9 (24.55 to 60.92)		

% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 9.74)	0.0 (0.00 to 11.22)		
% of subjects with HI titer ≥1:40 at Day 202	33.3 (18.56 to 50.97)	41.9 (24.55 to 60.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with HI titer ≥1:40 (HI assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 202.
Percentage of subjects achieving seroconversion with a titer of ≥1:40 on Day 202.

Subject Analysis Set: PPS Immunogenicity (3 years to <9 years age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	33	33
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	3.0 (0.08 to 15.76)	2.7 (0.07 to 14.16)	0.0 (0.00 to 10.58)	3.0 (0.08 to 15.76)
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	0.0 (0.00 to 9.49)	0.0 (0.00 to 10.58)	0.0 (0.00 to 10.58)
% of subjects with HI titer ≥1:40 at Day 202	3.0 (0.08 to 15.76)	2.7 (0.07 to 14.16)	0.0 (0.00 to 10.58)	3.0 (0.08 to 15.76)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	9.1 (1.92 to 24.33)	11.1 (3.11 to 26.06)		
% of subjects with HI titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	2.8 (0.07 to 14.53)		

% of subjects with HI titer ≥1:40 at Day 202	9.1 (1.92 to 24.33)	11.1 (3.11 to 26.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - GMTs and GMRs (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - GMTs and GMRs (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point description:

GMTs on Day 1 and Day 202 (6 months after the second vaccination) as determined by MN assay. GMRs calculated as follows: Day 202/Day 1 as determined by MN assay.

Subject Analysis Set: PPS Immunogenicity (overall study population)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71	67	66
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.19 (4.9 to 5.5)	5.27 (5.0 to 5.6)	5.38 (5.1 to 5.7)	5.16 (4.9 to 5.5)
GMT Day 202	113.24 (94.7 to 135.4)	146.98 (123.6 to 174.8)	146.41 (122.4 to 175.1)	150.56 (125.7 to 180.3)
GMR Day 202/Day 1	21.77 (18.1 to 26.1)	27.94 (23.4 to 33.4)	27.45 (22.9 to 33.0)	29.04 (24.2 to 34.9)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67[36]		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.13 (4.9 to 5.4)	5.31 (5.0 to 5.6)		
GMT Day 202	183.15 (153.6 to 218.4)	195.57 (163.3 to 234.2)		

GMR Day 202/Day 1	35.47 (29.6 to 42.5)	36.95 (30.7 to 44.4)		

Notes:

[36] - n=66 at Day 202

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 6 months to <36 months age cohort (PPS Immunogenicity)

End point description:

GMTs on Day 1 and Day 202 (6 months after the second vaccination) as determined by MN assay. GMRs calculated as follows: Day 202/Day 1 as determined by MN assay.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.00 (4.7 to 5.3)	5.00 (4.7 to 5.3)	5.26 (4.9 to 5.6)	5.21 (4.9 to 5.6)
GMT Day 202	144.60 (111.8 to 187.0)	217.84 (168.4 to 281.7)	175.31 (135.6 to 226.7)	174.21 (134.2 to 226.1)
GMR Day 202/Day 1	28.49 (22.0 to 36.9)	42.91 (33.2 to 55.5)	33.76 (26.1 to 43.7)	33.68 (25.9 to 43.7)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	31		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.10 (4.8 to 5.4)	5.29 (4.9 to 5.7)		
GMT Day 202	245.52 (191.3 to 315.1)	268.31 (205.0 to 351.3)		

GMR Day 202/Day 1	47.95 (37.3 to 61.6)	51.56 (39.4 to 67.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - GMTs and GMRs (MN assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point description:

GMTs on Day 1 and Day 202 (6 months after the second vaccination) as determined by MN assay. GMRs calculated as follows: Day 202/Day 1 as determined by MN assay.

Subject Analysis Set: PPS Immunogenicity (3 years to <9 years age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	33	33
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.38 (4.9 to 5.9)	5.54 (5.1 to 6.0)	5.49 (5.0 to 6.0)	5.11 (4.7 to 5.6)
GMT Day 202	89.38 (69.6 to 114.8)	101.19 (79.8 to 128.2)	122.19 (95.1 to 157.0)	129.11 (100.4 to 165.9)
GMR Day 202/Day 1	16.64 (12.8 to 21.6)	18.41 (14.4 to 23.5)	22.38 (17.3 to 29.0)	25.04 (19.3 to 32.5)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36[37]		
Units: Titer / ratio				
geometric mean (confidence interval 95%)				
GMT Day 1	5.16 (4.7 to 5.7)	5.35 (4.9 to 5.8)		
GMT Day 202	136.08 (105.9 to 174.9)	142.59 (111.8 to 181.8)		

GMR Day 202/Day 1	26.18 (20.2 to 34.0)	26.63 (20.7 to 34.3)		

Notes:

[37] - n=35 at Day 202

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the overall study population (PPS Immunogenicity)

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 202.
Percentage of subjects achieving seroconversion with a titer of ≥1:40 on Day 202.

Subject Analysis Set: PPS Immunogenicity (overall study population)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	71	67	66
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	95.5 (87.47 to 99.07)	97.2 (90.19 to 99.66)	100.0 (94.64 to 100.00)	97.0 (89.48 to 99.63)
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.06)	0.0 (0.00 to 5.36)	0.0 (0.00 to 5.44)
% of subjects with MN titer ≥1:40 at Day 202	95.5 (87.47 to 99.07)	98.6 (92.40 to 99.96)	100.0 (94.64 to 100.00)	97.0 (89.48 to 99.63)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67[38]		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	98.6 (92.19 to 99.96)	97.0 (89.48 to 99.63)		
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 5.21)	0.0 (0.00 to 5.36)		

% of subjects with MN titer ≥1:40 at Day 202	98.6 (92.19 to 99.96)	98.5 (91.84 to 99.96)		

Notes:

[38] - n=66 at Day 202

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 6 months to 36 months age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 6 months to 36 months age cohort (PPS Immunogenicity)

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 202.
Percentage of subjects achieving seroconversion with a titer of ≥1:40 on Day 202.

Subject Analysis Set: PPS Immunogenicity (6 months to <36 months age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	34	33
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	97.1 (84.67 to 99.93)	100.0 (89.72 to 100.00)	100.0 (89.72 to 100.00)	97.0 (84.24 to 99.92)
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.28)	0.0 (0.00 to 10.58)
% of subjects with MN titer ≥1:40 at Day 202	97.1 (84.67 to 99.93)	100.0 (89.72 to 100.00)	100.0 (89.72 to 100.00)	97.0 (84.24 to 99.92)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	31		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	100.0 (90.26 to 100.00)	100.0 (88.78 to 100.00)		

% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 9.74)	0.0 (0.00 to 11.22)		
% of subjects with MN titer ≥1:40 at Day 202	100.0 (90.26 to 100.00)	100.0 (88.78 to 100.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point title	Persistence of antibody responses at Day 202 - percentage of subjects with seroconversion and percentage of subjects with MN titer ≥1:40 (MN assay against the homologous H5N1 strain) in the 3 years to <9 years age cohort (PPS Immunogenicity)

End point description:

Percentage of subjects achieving seroconversion (non-detectable to ≥1:40, or 4-fold increase from a detectable Day 1 titer) on Day 202.
Percentage of subjects achieving seroconversion with a titer of ≥1:40 on Day 202.

Subject Analysis Set: PPS Immunogenicity (3 years to <9 years age cohort)

End point type	Secondary

End point timeframe:

Day 1 to Day 202

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	33	33
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	93.9 (79.77 to 99.26)	94.6 (81.81 to 99.34)	100.0 (89.42 to 100.00)	97.0 (84.24 to 99.92)
% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	0.0 (0.00 to 9.49)	0.0 (0.00 to 10.58)	0.0 (0.00 to 10.58)
% of subjects with MN titer ≥1:40 at Day 202	93.9 (79.77 to 99.26)	97.3 (85.84 to 99.93)	100.0 (89.42 to 100.00)	97.0 (84.24 to 99.92)

End point values	Arm E	Arm F		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36[39]		
Units: Percentage of subjects				
number (confidence interval 95%)				
% of subjects with seroconversion at Day 202	97.0 (84.24 to 99.92)	94.3 (80.84 to 99.30)		

% of subjects with MN titer ≥1:40 at Day 1	0.0 (0.00 to 10.58)	0.0 (0.00 to 9.74)		
% of subjects with MN titer ≥1:40 at Day 202	97.0 (84.24 to 99.92)	97.1 (85.08 to 99.93)		

Notes:

[39] - n=35 at Day 202

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 1 through Day 387	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0
Reporting groups	
Reporting group title	Arm A
Reporting group description: 1.875 µg H5N1 HA/50% MF59	
Reporting group title	Arm B
Reporting group description: 3.75 µg H5N1 HA/50% MF59	
Reporting group title	Arm C
Reporting group description: 7.5 µg H5N1 HA/50% MF59	
Reporting group title	Arm D
Reporting group description: 1.875 µg H5N1 HA/100% MF59	
Reporting group title	Arm E
Reporting group description: 3.75 µg H5N1 HA/100% MF59	
Reporting group title	Arm F
Reporting group description: 7.5 µg H5N1 HA/100% MF59	

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 69 (0.00%)	1 / 72 (1.39%)	3 / 70 (4.29%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	0 / 69 (0.00%)	1 / 72 (1.39%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Injury, poisoning and procedural complications			
Animal bite			

subjects affected / exposed	0 / 69 (0.00%)	0 / 72 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 69 (0.00%)	0 / 72 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 72 (0.00%)	0 / 70 (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			
Klebsiella infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 72 (1.39%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 72 (0.00%)	0 / 70 (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
Septic shock			
subjects affected / exposed	0 / 69 (0.00%)	1 / 72 (1.39%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm D	Arm E	Arm F
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 70 (0.00%)	1 / 69 (1.45%)	3 / 70 (4.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			

subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 70 (0.00%)	1 / 69 (1.45%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Klebsiella infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 70 (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 / 70 (0.00%)	1 / 69 (1.45%)	0 / 70 (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
Septic shock			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 70 (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

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

Non-serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 69 (10.14%)	4 / 72 (5.56%)	14 / 70 (20.00%)
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	6 / 69 (8.70%)	4 / 72 (5.56%)	12 / 70 (17.14%)
occurrences (all)	6	4	13
Nasopharyngitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 72 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2

Non-serious adverse events	Arm D	Arm E	Arm F
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 70 (7.14%)	5 / 69 (7.25%)	9 / 70 (12.86%)
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 70 (1.43%)	5 / 69 (7.25%)	5 / 70 (7.14%)
occurrences (all)	1	5	5
Nasopharyngitis			
subjects affected / exposed	4 / 70 (5.71%)	0 / 69 (0.00%)	4 / 70 (5.71%)
occurrences (all)	4	0	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2019	Version 1.0 to Version 2.0 The main reasons for the protocol amendment were the following: 1. Removal of the cohort of adolescents aged 9 years to <18 years of age, such that the age range of the study population is 6 months to <9 years. In line with this change, all subjects were scheduled to receive 2 doses of vaccine in the study, instead of 1 or 2 doses, based on the subject's age. 2. Removal of the vaccine group that was planned to receive a single dose of study vaccine on Day 1 and saline placebo on Day 22. In line with this change, the overall sample size was reduced from 450 subjects to 420 subjects. Removal of the antigenic challenge dose of non-adjuvanted 7.5 µg H5N1 pandemic influenza antigen planned for all subjects on Day 202. 3. Reduction in the number of blood samples collected, from blood samples being collected on Day 1, Day 22, Day 43, Day 204, and Day 225 to blood samples being collected on Day 1, Day 22, Day 43, and Day 202. 4. Removal of CMI testing as an exploratory objective. 5. Reduction in the number of clinic visits/calls. 6. Alignment of objectives/endpoints with the key binding elements of PIP.
07 November 2019	Version 2.0 to Version 3.0 The main reasons for the protocol amendment were the following: 1. Changes in vaccine formulation, necessitating updating of the description of the dose formulation to reflect the correct volume to be used as reference for vaccine label documentation. Specifically, the description of the dose for Arm C was changed from "7.5 µg + 50% MF59 0.5 mL" to "7.5 µg + 50% MF59 0.25 mL". 2. Updating the Time and Events table to provide clarification on prevaccination/Visit 1 procedures, including addition of explanatory footnotes.
20 December 2019	Version 3.0 to Version 4.0 The main reasons for the protocol amendment were the following: 1. Addition of collection of a baseline blood sample within 10 days prior to the Day 1 vaccination as an inclusion criterion. This change was made because assessment of two of the primary endpoints requires a baseline blood sample. The burden of the study for subjects in the age range 6 months to <9 years of age without a baseline blood sample, who would not be included in the evaluation of these primary endpoints, was considered unreasonable. In line with this change, the timing of the collection of the baseline blood sample was changed from "before vaccination" to "before randomization". 2. Deletion of the restricted use of antiviral medication with anti-flu properties.
24 June 2020	Version 4.0 to Version 5.0 The main reasons for the protocol amendment were the following: 1. Introduction of the possibility of home visits to mitigate risks associated with the SARS-CoV-2 pandemic. In the exceptional case that the site staff was not able to perform visits at the clinic due to COVID-19 restrictions, home visits (physical examination and blood draw) could be considered. These visits would only be considered if sites had appropriate SOPs/Instructions for conducting home visits in place, reviewed, and approved by Seqirus. In addition, sites had to instruct subjects on return of the Subject Diary Card if a clinic visit was not feasible. 2. Introduction of the permitted use of a topical analgesic/anesthetic/icepack to reduce the discomfort and pain of the blood draws in this pediatric study, as a mitigation strategy for non-compliance with blood draws.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported