



Clinical trial results:

A Phase 2/3, randomized, controlled, observer-blind, multi-center trial to evaluate the safety and immunogenicity of a two-dose primary vaccination series of monovalent A/Indonesia/5/2005 (H5N1) vaccine antigen adjuvanted with AS03 in children aged 6 months to < 18 years of age.

Summary

EudraCT number	2012-001683-29
Trial protocol	Outside EU/EEA
Global end of trial date	26 January 2014

Results information

Result version number	v1
This version publication date	02 May 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	114464
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01310413
WHO universal trial number (UTN)	-
Other trial identifiers	HHS O100200700029C: HHS/BARDA Contract Number

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trails Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trails Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 July 2011
Global end of trial reached?	Yes
Global end of trial date	26 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether two doses of H5N1 antigen in association with AS03 adjuvant elicits an immune response, measured by postimmunization vaccine-homologous virus hemagglutination inhibition (HI) titers, that meets or exceeds Center for Biologics Evaluation and Research (CBER)/ Committee for Medicinal Products for Human Use (CHMP) young adult targets for proportion of subjects attaining postimmunization reciprocal HI titres ≥ 40 against A/Indonesia/5/2005 virus (abbreviated seroprotection rate [SPR]).

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 453
Country: Number of subjects enrolled	Thailand: 292
Country: Number of subjects enrolled	Canada: 97
Worldwide total number of subjects	842
EEA total number of subjects	0

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)	274
Children (2-11 years)	568
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:

The study included a first 385-days Blinded Phase (all subjects), followed by a 385-days Unblinded Phase. In this phase, subjects who received the placebo in the Blinded Phase were offered, after completing the Blinded Phase, 2 doses of Influenza A (H5N1) Virus monovalent vaccine administered for Dose 1 within a short delay of Day 385 (Day U0).

Pre-assignment

Screening details:

A total of 842 subjects were enrolled in the study in its Blinded Phase part. This number was later amended down to 838, following corrections for wrong subject number allocation and randomization errors.

Period 1

Period 1 title	Day 0 to Day 385
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Influenza A (H5N1) adjuvanted 6-<36M Group

Arm description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Arm type	Experimental
Investigational medicinal product name	Influenza A (H5N1) Virus monovalent vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

Arm title	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group
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Arm description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Arm type	Experimental
Investigational medicinal product name	Influenza A (H5N1) Virus monovalent vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

Arm title	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group
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Arm description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Arm type	Experimental
Investigational medicinal product name	Influenza A (H5N1) Virus monovalent vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

Arm title	Placebo 6-<36M Group
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Arm description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Arm type	Active comparator
Investigational medicinal product name	Saline placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

Arm title	Placebo 3-<9Y Group
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Arm description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Arm type	Active comparator
Investigational medicinal product name	Saline placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

Arm title	Placebo 9-<18Y Group
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Arm description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of saline

placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Arm type	Active comparator
Investigational medicinal product name	Saline placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

Number of subjects in period 1 ^[1]	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group
Started	199	198	210
Completed	172	190	203
Not completed	27	8	7
Consent withdrawn by subject	5	2	-
Migrated/moved from study are	3	3	1
Unspecified	1	-	3
Lost to follow-up	18	3	3

Number of subjects in period 1 ^[1]	Placebo 6-<36M Group	Placebo 3-<9Y Group	Placebo 9-<18Y Group
Started	75	76	80
Completed	67	73	77
Not completed	8	3	3
Consent withdrawn by subject	2	1	1
Migrated/moved from study are	1	1	-
Unspecified	-	-	-
Lost to follow-up	5	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 842 subjects were enrolled in the study in its Blinded Phase part. This number was later amended down to 838, following corrections for wrong subject number allocation and randomization errors.

Period 2

Period 2 title	Day Uo to Day U385
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Placebo/Influenza A (H5N1) Adjuvanted Group
Arm description:	
Subjects in this group were those who were administered the saline placebo solution in the Blinded Phase of the study (either in the Placebo 6-<36M, Placebo 3-<9Y or Placebo 9-<18Y Group). These were subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who had received 2 doses of saline placebo at Days 0 and 21 in the Blinded Phase of the study, as per described in the descriptions of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups. After consenting to participating to the Unblinded Phase of the study, these subjects received in addition 2 doses of Influenza A (H5N1) Virus monovalent vaccine at Days 385 (Day U0) and Day 385 + 21 days (Day U21). Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. Dose 1 was administered in the deltoid region of the non-dominant arm and Dose 2 in the deltoid region of the dominant arm.	
Arm type	Experimental
Investigational medicinal product name	Influenza A (H5N1) Virus monovalent vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
All subjects will receive 2 doses administered as an intramuscular (IM) injection at Days U0 and U21.	

Number of subjects in period 2^[2]	Placebo/Influenza A (H5N1) Adjuvanted Group
Started	155
Completed	152
Not completed	3
Consent withdrawn by subject	1
Lost to follow-up	2

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of the 782 subjects aged 6 months to <18 years that completed the Blinded phase of the study (Day 0 to Day 385), only 155 subjects consented to participate in the Unblinded phase of the study (Day U0 to Day U385). Thus, the number of subjects starting the period is not consistent with the number completing the preceding period.

Baseline characteristics

Reporting groups

Reporting group title	Influenza A (H5N1) adjuvanted 6-<36M Group
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Reporting group description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (\geq) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group title	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group
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Reporting group description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group title	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group
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Reporting group description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group title	Placebo 6-<36M Group
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Reporting group description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (\geq) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group title	Placebo 3-<9Y Group
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Reporting group description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group title	Placebo 9-<18Y Group
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Reporting group description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group
Number of subjects	199	198	210
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	21.7	70.5	160.8
standard deviation	± 8.17	± 21.71	± 28.21
Gender categorical Units: Subjects			
Female	92	90	103
Male	107	108	107

Reporting group values	Placebo 6-<36M Group	Placebo 3-<9Y Group	Placebo 9-<18Y Group
Number of subjects	75	76	80
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	22.6	65.2	156
standard deviation	± 8.17	± 20.2	± 31.29
Gender categorical Units: Subjects			
Female	39	35	42
Male	36	41	38

Reporting group values	Total		
Number of subjects	838		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		

Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: months arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	401		
Male	437		

End points

End points reporting groups

Reporting group title	Influenza A (H5N1) adjuvanted 6-<36M Group
Reporting group description: Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).	
Reporting group title	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group
Reporting group description: Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).	
Reporting group title	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group
Reporting group description: Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).	
Reporting group title	Placebo 6-<36M Group
Reporting group description: Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).	
Reporting group title	Placebo 3-<9Y Group
Reporting group description: Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).	
Reporting group title	Placebo 9-<18Y Group
Reporting group description: Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).	
Reporting group title	Placebo/Influenza A (H5N1) Adjuvanted Group
Reporting group description: Subjects in this group were those who were administered the saline placebo solution in the Blinded Phase of the study (either in the Placebo 6-<36M, Placebo 3-<9Y or Placebo 9-<18Y Group). These were subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who had received 2 doses of saline placebo at Days 0 and 21 in the Blinded Phase of the study, as per described in the descriptions of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups. After consenting to participating to the Unblinded Phase of the study, these subjects received in addition 2 doses of Influenza A (H5N1) Virus monovalent vaccine at Days 385 (Day U0) and Day 385 + 21 days (Day U21). Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. Dose 1 was administered in the deltoid region of the non-dominant arm and Dose 2 in the deltoid region of the dominant arm.	

Subject analysis set title	Influenza A (H5N1) adjuvanted Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This group results from the pooling of the Influenza A (H5N1) adjuvanted 6-<36M, Influenza A (H5N1) adjuvanted 3-<9Y and Influenza A (H5N1) adjuvanted months and 18 years, 18 years excluded, who received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (\geq) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Subject analysis set title	Placebo Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

This group results from the pooling of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups and includes subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who received 2 doses of 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (\geq) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Primary: Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point title	Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain. ^[1]
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End point description:

A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40.

End point type	Primary
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End point timeframe:

At Day 42.

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	175	185	203	64
Units: Subjects				
A/INDO, Day 42	175	184	201	0

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Subjects				

A/INDO, Day 42	0	1		
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Statistical analyses

No statistical analyses for this end point

Primary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain

End point title	Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain ^[2]
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End point description:

HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10.

End point type	Primary
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End point timeframe:

At Day 42.

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Influenza A (H5N1) adjuvanted 6- <36M Group	Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group	Placebo 6- <36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	175	185	203	64
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 42	777.1 (705.6 to 855.9)	543.8 (484.9 to 609.8)	416.2 (371.5 to 466.2)	5.1 (4.9 to 5.3)

End point values	Placebo 3- <9Y Group	Placebo 9- <18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 42	5.4 (5 to 5.7)	5.8 (5.3 to 6.3)		

Statistical analyses

Secondary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point title	Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.
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End point description:

HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10.

End point type	Secondary
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End point timeframe:

At Days 0 and 21

End point values	Influenza A (H5N1) adjuvanted 6- <36M Group	Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group	Placebo 6- <36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	182	184	204	67
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=182;184;204;67;71;76]	5.3 (5.1 to 5.5)	5.6 (5.3 to 5.9)	5.7 (5.4 to 6.1)	5.3 (5 to 5.7)
A/INDO, Day 21 [N=179;184;204;67;70;76]	38.7 (33.9 to 44.2)	44.6 (39.2 to 50.9)	35.3 (31.7 to 39.5)	5.2 (5 to 5.4)

End point values	Placebo 3- <9Y Group	Placebo 9- <18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=182;184;204;67;71;76]	5.6 (5.1 to 6)	5.4 (5.1 to 5.8)		
A/INDO, Day 21 [N=179;184;204;67;70;76]	5.4 (5 to 5.7)	5.4 (5.1 to 5.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point title	Number of subjects seroprotected for haemagglutination
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inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point description:

A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40.

End point type Secondary

End point timeframe:

At Days 0 and 21

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	182	184	204	67
Units: Subjects				
A/INDO, Day 0 [N=182;184;204;67;71;76]	1	2	1	0
A/INDO, Day 21 [N=179;184;204;67;70;76]	105	110	108	0

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Subjects				
A/INDO, Day 0 [N=182;184;204;67;71;76]	0	0		
A/INDO, Day 21 [N=179;184;204;67;70;76]	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point title Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point description:

A subject seroconverted for HI antibodies against the H5N1 A/Indonesia virus strain (A/INDO) was defined as a vaccinee with either a pre-vaccination titer less than ($<$) 1:10 and a post-vaccination titer higher than or equal to (\geq) 1:40, or with a pre-vaccination titer \geq 1:10 and at least a 4-fold increase in post-vaccination titer.

End point type	Secondary
End point timeframe:	
At Days 21 and 42	

End point values	Influenza A (H5N1) adjuvanted 6- <36M Group	Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group	Placebo 6- <36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	179	185	204	67
Units: Subjects				
A/INDO, Day 21 [N=179;184;204;67;70;76]	103	107	105	0
A/INDO, Day 42 [N=175;185;203;64;71;76]	175	183	201	0

End point values	Placebo 3- <9Y Group	Placebo 9- <18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Subjects				
A/INDO, Day 21 [N=179;184;204;67;70;76]	0	0		
A/INDO, Day 42 [N=175;185;203;64;71;76]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point title	Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.
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End point description:

GMI also known as the seroconversion factor (SCF) or geometric mean fold rise (GMFR) was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination reciprocal HI titre for the vaccine virus.

End point type	Secondary
End point timeframe:	
At Days 21 and 42	

End point values	Influenza A (H5N1) adjuvanted 6- <36M Group	Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group	Placebo 6- <36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	179	185	204	67
Units: Ratio				
geometric mean (confidence interval 95%)				
A/INDO, Day 21 [N=179;184;204;67;70;76]	7.3 (6.4 to 8.4)	8 (7 to 9.1)	6.2 (5.5 to 6.9)	1 (0.9 to 1)
A/INDO, Day 42 [N=175;185;203;64;71;76]	148.5 (134.5 to 164.1)	96.9 (85.3 to 110.1)	72.4 (63.9 to 82)	1 (0.9 to 1)

End point values	Placebo 3- <9Y Group	Placebo 9- <18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Ratio				
geometric mean (confidence interval 95%)				
A/INDO, Day 21 [N=179;184;204;67;70;76]	1 (0.9 to 1)	1 (0.9 to 1)		
A/INDO, Day 42 [N=175;185;203;64;71;76]	1 (0.9 to 1)	1.1 (1 to 1.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point title	Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.
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End point description:

HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10.

End point type	Secondary
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End point timeframe:

At Day 0 and Day 182.

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	101	100	36
Units: Titre				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=107;101;100;36;37;35]	5.1 (5 to 5.2)	5.2 (5 to 5.4)	5.6 (5.2 to 6)	5.3 (4.9 to 5.7)
A/INDO, Day 182 [N=84;89;87;29;34;31]	90.6 (78.1 to 105)	57.4 (50.8 to 64.9)	50.2 (43.3 to 58.2)	5 (5 to 5)

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	35		
Units: Titre				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=107;101;100;36;37;35]	5.2 (4.8 to 5.8)	5.4 (4.8 to 6)		
A/INDO, Day 182 [N=84;89;87;29;34;31]	5.4 (4.9 to 6)	5.4 (4.9 to 5.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point title	Number of subjects seroprotected as regards haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.
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End point description:

A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40.

End point type	Secondary
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End point timeframe:

At Day 0 and Day 182

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	182	184	204	67
Units: Subjects				
A/INDO, Day 0 [N=182,184,204,67,71,76]	1	2	1	0
A/INDO, Day 182 [N=84;89;87;29;34;31]	80	75	63	0

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Subjects				
A/INDO, Day 0 [N=182,184,204,67,71,76]	0	0		
A/INDO, Day 182 [N=84;89;87;29;34;31]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point title	Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.
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End point description:

A subject seroconverted for HI antibodies against the H5N1 A/Indonesia virus strain (A/INDO) was defined as a vaccinee with either a pre-vaccination titer less than (<) 1:10 and a post-vaccination titer higher than or equal to (>=) 1:40, or with a pre-vaccination titer >= 1:10 and at least a 4-fold increase in post-vaccination titer.

End point type	Secondary
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End point timeframe:

At Day 182

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	89	87	29
Units: Subjects				

A/INDO	80	75	61	0
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End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	31		
Units: Subjects				
A/INDO	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point title	Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.
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End point description:

GMI also known as the seroconversion factor (SCF) or geometric mean fold rise (GMFR) was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination reciprocal HI titre for the vaccine virus.

End point type	Secondary
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End point timeframe:

At Day 182

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	89	87	29
Units: Ratio				
geometric mean (confidence interval 95%)				
A/INDO	17.8 (15.3 to 20.8)	11 (9.7 to 12.4)	8.8 (7.5 to 10.4)	1 (0.9 to 1)

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	31		
Units: Ratio				
geometric mean (confidence interval				

95%)				
A/INDO	1.1 (1 to 1.2)	1 (0.9 to 1.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point title	Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.
End point description: HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10.	
End point type	Secondary
End point timeframe: At Day 0 and Day 385	

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	182	184	204	67
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=182,184,204,67,71,76]	5.3 (5.1 to 5.5)	5.6 (5.3 to 5.9)	5.7 (5.4 to 6.1)	5.3 (5 to 5.7)
A/INDO, Day 385 [N=63;85;95;26;34;36]	65.6 (55.9 to 76.9)	32.8 (28.1 to 38.4)	21.6 (18.6 to 25.1)	5.1 (4.9 to 5.4)

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=182,184,204,67,71,76]	5.6 (5.1 to 6)	5.4 (5.1 to 5.8)		
A/INDO, Day 385 [N=63;85;95;26;34;36]	5.4 (4.9 to 5.8)	5.3 (4.8 to 5.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point title	Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.
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End point description:

A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40.

End point type	Secondary
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End point timeframe:

At Day 0 and Day 385

End point values	Influenza A (H5N1) adjuvanted 6- <36M Group	Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group	Placebo 6- <36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	182	184	204	67
Units: Subjects				
A/INDO, Day 0 [N=182, 184,204,67,71,76]	1	2	1	0
A/INDO, Day 385 [N=63;85;95;26;34;36]	54	47	27	0

End point values	Placebo 3- <9Y Group	Placebo 9- <18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	76		
Units: Subjects				
A/INDO, Day 0 [N=182, 184,204,67,71,76]	0	0		
A/INDO, Day 385 [N=63;85;95;26;34;36]	0	0		

Statistical analyses

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point title	Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.
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End point description:

A subject seroconverted for HI antibodies against the H5N1 A/Indonesia virus strain (A/INDO) was defined as a vaccinee with either a pre-vaccination titer less than ($<$) 1:10 and a post-vaccination titer higher than or equal to (\geq) 1:40, or with a pre-vaccination titer \geq 1:10 and at least a 4-fold increase in post-vaccination titer.

End point type	Secondary
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End point timeframe:

At Day 385

End point values	Influenza A (H5N1) adjuvanted 6- <36M Group	Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group	Placebo 6- <36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	84	95	26
Units: Subjects				
A/INDO	53	45	23	0

End point values	Placebo 3- <9Y Group	Placebo 9- <18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	36		
Units: Subjects				
A/INDO	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point title	Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.
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End point description:

GMI also known as the seroconversion factor (SCF) or geometric mean fold rise (GMFR) was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the pre-vaccination reciprocal HI titer for the vaccine virus.

End point type	Secondary
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End point timeframe:

At Day 385.

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	85	95	26
Units: Fold increase				
geometric mean (confidence interval 95%)				
Fold increase	12.1 (10.3 to 14.2)	5.5 (4.7 to 6.6)	3.6 (3.1 to 4.3)	1 (0.9 to 1.1)

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	36		
Units: Fold increase				
geometric mean (confidence interval 95%)				
Fold increase	0.9 (0.8 to 1)	1 (0.8 to 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Microneutralization (MN) antibody titers against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains.

End point title	Microneutralization (MN) antibody titers against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains.
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End point description:

MN HI antibody titers against the H5N1 A/Indonesia (A/INDO) and H5N1 A/Vietnam (A/VIET) virus strains were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:28.

End point type	Secondary
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End point timeframe:

At Days 0, 42, 182 and 385

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	39	40	10
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=36;37;40;7;10;11]	14 (14 to 14)	15.67 (14.37 to 17.08)	15.54 (14.13 to 17.09)	15.46 (12.13 to 19.7)
A/INDO, Day 42 [N=34;37;40;6;10;11]	855.62 (597.88 to 1224.47)	657.6 (453.13 to 954.33)	380.62 (277.43 to 522.2)	14 (14 to 14)
A/INDO, Day 182 [N=33;39;33;10;10;9]	216.82 (162.03 to 290.14)	130.32 (107.3 to 158.26)	104.18 (86.95 to 124.82)	16.11 (11.73 to 22.13)
A/INDO, Day 385 [N=25;33;37;8;11;9]	166.64 (135.9 to 204.32)	108.59 (87.88 to 134.19)	82.26 (67.27 to 100.59)	15.27 (12.44 to 18.74)
A/VIET, Day 0 [N=36;36;40;7;10;11]	14.83 (13.89 to 15.84)	19.84 (16.82 to 23.4)	24.88 (20.75 to 29.85)	17.11 (10.47 to 27.95)
A/VIET, Day 42 [N=34;37;40;6;10;11]	68.18 (58.05 to 80.07)	71.15 (61.62 to 82.15)	65.25 (57.03 to 74.64)	17.69 (9.69 to 32.28)
A/VIET, Day 182 [N=33;39;33;10;10;9]	48.77 (36.56 to 65.06)	44.11 (36.19 to 53.77)	61.67 (51.38 to 74.01)	19.82 (12.22 to 32.14)
A/VIET, Day 385 [N=25;33;37;8;11;9]	59.83 (48.09 to 74.43)	38.62 (30.6 to 48.73)	47.73 (38.76 to 58.79)	14 (14 to 14)

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Titer				
geometric mean (confidence interval 95%)				
A/INDO, Day 0 [N=36;37;40;7;10;11]	14 (14 to 14)	14.91 (12.96 to 17.16)		
A/INDO, Day 42 [N=34;37;40;6;10;11]	14 (14 to 14)	14.91 (12.96 to 17.16)		
A/INDO, Day 182 [N=33;39;33;10;10;9]	14 (14 to 14)	17.67 (12.08 to 25.86)		
A/INDO, Day 385 [N=25;33;37;8;11;9]	14.91 (12.96 to 17.16)	16.33 (12.91 to 20.66)		
A/VIET, Day 0 [N=36;36;40;7;10;11]	16.08 (13.05 to 19.82)	20.47 (14.82 to 28.26)		
A/VIET, Day 42 [N=34;37;40;6;10;11]	19.87 (12.97 to 30.43)	28.14 (19.53 to 40.54)		
A/VIET, Day 182 [N=33;39;33;10;10;9]	17.24 (13.56 to 21.9)	24.14 (14.29 to 40.78)		
A/VIET, Day 385 [N=25;33;37;8;11;9]	18.07 (12.34 to 26.47)	35.42 (19.45 to 64.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine response rate (VRR) for microneutralization (MN) antibodies against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains.

End point title	Vaccine response rate (VRR) for microneutralization (MN) antibodies against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains.
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End point description:

A subject with a vaccine response was defined either as a seronegative subject with an antibody titre < 1:28 for H5N1 Flu A/Indonesia MN and H5N1 A/Vietnam or as a seropositive subject with an antibody titre ≥ 1:28 for H5N1 Flu A/Indonesia MN and H5N1 A/Vietnam.

End point type	Secondary
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End point timeframe:

At Day 42

End point values	Influenza A (H5N1) adjuvanted 6- <36M Group	Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group	Placebo 6- <36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	37	40	6
Units: Subjects				
A/INDO [N=34;37;40;6;10;11]	34	37	39	0
A/VIET [N=34;36;40;6;10;11]	30	26	16	0

End point values	Placebo 3- <9Y Group	Placebo 9- <18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Subjects				
A/INDO [N=34;37;40;6;10;11]	0	0		
A/VIET [N=34;36;40;6;10;11]	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms.

End point title	Number of subjects reporting solicited local symptoms.
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End point description:

Solicited local symptoms assessed were pain, redness and swelling. "Any" was defined as any occurrence of the specified solicited local symptom reported, regardless of intensity. Grade 3 pain was defined as pain that prevented normal activity. Grade 3 redness and swelling were defined as redness/swelling above 100 millimeter (mm). As the study is still ongoing and data per age group are not available, results are presented for the groups pooled by vaccine/placebo administered. This outcome measure will be amended when data by age group become available.

End point type	Secondary
End point timeframe:	
During the 7-day (Days 0-6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses	

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	603	229		
Units: Subjects				
Any pain	405	69		
Grade 3 pain	25	4		
Any redness	29	0		
Grade 3 redness	1	0		
Any swelling	41	1		
Grade 3 swelling	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms.

End point title	Number of subjects reporting solicited local symptoms.
End point description:	
Solicited local symptoms assessed were pain and swelling. "Any" was defined as any occurrence of the specified solicited local symptom reported, regardless of intensity. Grade 3 pain was defined as pain that prevented normal activity. Grade 3 redness and swelling were defined as redness/swelling above 100 millimeter (mm). As the study is still ongoing and data per age group are not available, results are presented for the groups pooled by vaccine/placebo administered. This outcome measure will be amended when data by age group become available.	
End point type	Secondary
End point timeframe:	
During the 7-day (Days U0-U6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses	

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: Subjects				
Any Pain	111			
Grade 3 Pain	8			
Any Redness	6			

Grade 3 Redness	0			
Any Swelling	5			
Grade 3 Swelling	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects of less than 6 years of age reporting solicited general symptoms.

End point title	Number of subjects of less than 6 years of age reporting solicited general symptoms.
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End point description:

Solicited general symptoms assessed in subjects of less than 6 years of age were drowsiness, irritability/fussiness, loss of appetite and fever [axillary temperature (T) higher than or equal to (\geq) 38.0 degrees Celsius ($^{\circ}\text{C}$)]. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination. Any fever was defined as axillary temperature above 38.0 degrees Celsius ($^{\circ}\text{C}$). Grade 3 fever was axillary temperature above 39.0 $^{\circ}\text{C}$.

End point type	Secondary
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End point timeframe:

During the 7-day (Days 0-6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	122		
Units: Subjects				
Any Drowsiness	101	29		
Grade 3 Drowsiness	9	2		
Related Drowsiness	81	21		
Any Irritability/fussiness	128	40		
Grade 3 Irritability/fussiness	10	2		
Related Irritability/fussiness	111	33		
Any Loss of appetite	79	29		
Grade 3 Loss of appetite	8	4		
Related Loss of appetite	63	20		
Any Fever (Axillary T \geq 38.0 $^{\circ}\text{C}$)	59	21		
Grade 3 Fever	14	5		
Related Fever	41	14		

Statistical analyses

Secondary: Number of subjects of less than 6 years of age reporting solicited general symptoms.

End point title	Number of subjects of less than 6 years of age reporting solicited general symptoms.
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End point description:

Solicited general symptoms assessed in subjects of less than 6 years of age were drowsiness, irritability/fussiness, loss of appetite and fever [axillary temperature (T) higher than or equal to (\geq) 38.0 degrees Celsius ($^{\circ}\text{C}$)]. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination. Any fever was defined as axillary temperature above 38.0 degrees Celsius ($^{\circ}\text{C}$). Grade 3 fever was axillary temperature above 39.0 $^{\circ}\text{C}$.

End point type	Secondary
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End point timeframe:

During the 7-day (Days U0-U6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, for each dose

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Subjects				
Any Drowsiness	23			
Grade 3 Drowsiness	1			
Related Drowsiness	17			
Any Irritability/Fussiness	28			
Grade 3 Irritability/Fussiness	1			
Related Irritability/Fussiness	23			
Any Loss of appetite	18			
Grade 3 Loss of appetite	0			
Related Loss of appetite	13			
Any Fever	4			
Grade 3 Fever	2			
Related Fever	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects at least 6 years of age reporting solicited general symptoms.

End point title	Number of subjects at least 6 years of age reporting solicited general symptoms.
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End point description:

Solicited general symptoms assessed in subjects of at least 6 years of age were fatigue, gastrointestinal symptoms, headache, joint pain at other location, muscle aches, shivering, sweating and fever [axillary

temperature (T) ≥ 38.0 degrees Celsius ($^{\circ}\text{C}$)]. Gastrointestinal symptoms included nausea, vomiting, diarrhea and/or abdominal pain. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

During the 7-day (Days 0-6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	309	107		
Units: Subjects				
Any fatigue	89	19		
Grade 3 fatigue	4	2		
Related fatigue	77	16		
Any gastrointestinal symptoms	43	18		
Grade 3 gastrointestinal symptoms	4	2		
Related gastrointestinal symptoms	27	11		
Any headache	100	18		
Grade 3 headache	8	3		
Related headache	87	15		
Any joint pain	50	9		
Grade 3 joint pain	2	0		
Related joint pain	43	8		
Any muscle aches	123	17		
Grade 3 muscle aches	7	1		
Related muscle aches	114	14		
Any shivering	25	7		
Grade 3 shivering	2	1		
Related shivering	19	5		
Any sweating	25	4		
Grade 3 sweating	2	0		
Related sweating	22	1		
Any fever [axillary temperature $\geq 38.0^{\circ}\text{C}$]	19	3		
Grade 3 fever	5	1		
Related fever	13	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects at least 6 years of age reporting solicited general symptoms.

End point title	Number of subjects at least 6 years of age reporting solicited general symptoms.
End point description:	
Solicited general symptoms assessed in subjects of at least 6 years of age were fatigue, gastrointestinal symptoms, headache, joint pain at other location, muscle aches, shivering, sweating and fever [axillary temperature (T) ≥ 38.0 degrees Celsius ($^{\circ}\text{C}$)]. Gastrointestinal symptoms included nausea, vomiting, diarrhea and/or abdominal pain. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination.	
End point type	Secondary
End point timeframe:	
During the 7-day (Days U0-U6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, for each dose	

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Subjects				
Any Fatigue	18			
Grade 3 Fatigue	1			
Related Fatigue	13			
Any Gastrointestinal	7			
Grade 3 Gastrointestinal	0			
Related Gastrointestinal	5			
Any Headache	24			
Grade 3 Headache	1			
Related Headache	20			
Any Increased Sweating	5			
Grade 3 Increased Sweating	0			
Related Increased Sweating	3			
Any Joint Pain	14			
Grade 3 Joint Pain	0			
Related Joint Pain	12			
Any Muscle Aches	34			
Grade 3 Muscle Aches	0			
Related Muscle Aches	28			
Any Shivering (Chills)	7			
Grade 3 Shivering (Chills)	2			
Related Shivering (Chills)	4			
Any Fever	1			
Grade 3 Fever	0			
Related Fever	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically-attended adverse events (MAEs)

End point title	Number of subjects with medically-attended adverse events (MAEs)
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End point description:

MAEs were defined as adverse events with medically-attended visits that were not routine visits for physical examination or vaccination. Any MAE was defined as at least 1 MAE experienced.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
Subject(s) with any MAE(s)	189	77		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically-attended adverse events (MAEs)

End point title	Number of subjects with medically-attended adverse events (MAEs)
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End point description:

MAEs were defined as adverse events with medically-attended visits that were not routine visits for physical examination or vaccination. Any MAE was defined as at least 1 MAE experienced.

End point type	Secondary
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End point timeframe:

From Day U0 up to Day U385

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Subjects				
Any MAEs	36			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential Immune-Mediated Diseases (pIMDs)

End point title	Number of subjects with any potential Immune-Mediated Diseases (pIMDs)
End point description: Potential immune-mediated diseases (pIMDs) were defined as a subset of adverse events that included both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which might or might not have an autoimmune aetiology. "Any pIMD" was defined as at least one pIMD experienced by the study subject.	
End point type	Secondary
End point timeframe: From Day 0 up to Day 385	

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
Subject(s) with any pIMD(s)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential Immune-Mediated Diseases (pIMDs)

End point title	Number of subjects with any potential Immune-Mediated Diseases (pIMDs)
End point description: Potential immune-mediated diseases (pIMDs) were defined as a subset of adverse events that included both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which might or might not have an autoimmune aetiology. "Any pIMD" was defined as at least one pIMD experienced by the study subject.	
End point type	Secondary
End point timeframe: From Day U0 to Day U385	

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Subjects				
Subjects with any pIMD(s)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting pregnancies, and outcomes of these reported pregnancies

End point title	Number of subjects reporting pregnancies, and outcomes of these reported pregnancies
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End point description:

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
Subject(s) with any pregnancy	2	0		
Subject(s) with related pregnancy	0	0		
Spontaneous abortion	1	0		
Healthy live birth	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting pregnancies, and outcomes of these reported pregnancies

End point title	Number of subjects reporting pregnancies, and outcomes of these reported pregnancies
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End point description:

End point type	Secondary
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End point timeframe:

Up to Day U385

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Subjects				
Subject(s) with any pregnancy	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal biochemical parameters assessed with respect to alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT)

End point title	Number of subjects with normal and abnormal biochemical parameters assessed with respect to alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT)
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End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	606	231		
Units: Subjects				
ALAT, PRE Unknown [N=606,231]	15	4		
ALAT, PRE Below [N=606,231]	0	0		
ALAT, PRE Normal [N=606,231]	586	221		
ALAT, PRE Above [N=606,231]	5	6		
ALAT, Day 42 Unknown [N=583,220]	17	4		
ALAT, Day 42 Below [N=583,220]	0	0		
ALAT, Day 42 Normal [N=583,220]	562	212		

ALAT, Day 42 Above [N=583,220]	4	4		
ALAT, Day 182 Unknown [N=304,110]	6	0		
ALAT, Day 182 Below [N=304,110]	0	0		
ALAT, Day 182 Normal [N=304,110]	289	110		
ALAT, Day 182 Above [N=304,110]	9	0		
ALAT, Day 385 Unknown [N=251,104]	5	0		
ALAT, Day 385 Below [N=251,104]	0	0		
ALAT, Day 385 Normal [N=251,104]	245	100		
ALAT, Day 385 Above [N=251,104]	1	4		
ASAT, PRE Unknown [N=606,231]	15	4		
ASAT, PRE Below [N=606,231]	0	0		
ASAT, PRE Normal [N=606,231]	577	219		
ASAT, PRE Above [N=606,231]	14	8		
ASAT, Day 42 Unknown [N=583,220]	19	4		
ASAT, Day 42 Below [N=583,220]	0	0		
ASAT, Day 42 Normal [N=583,220]	552	208		
ASAT, Day 42 Above [N=583,220]	12	8		
ASAT, Day 182 Unknown [N=304,110]	8	0		
ASAT, Day 182 Below [N=304,110]	0	0		
ASAT, Day 182 Normal [N=304,110]	284	108		
ASAT, Day 182 Above [N=304,110]	12	2		
ASAT, Day 385 Unknown [N=251,104]	7	0		
ASAT, Day 385 Below [N=251,104]	0	0		
ASAT, Day 385 Normal [N=251,104]	240	100		
ASAT, Day 385 Above [N=251,104]	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal biochemical parameters assessed with respect to total bilirubin (T-BIL) and bilirubin conjugated/direct (BIL-C/D)

End point title	Number of subjects with normal and abnormal biochemical parameters assessed with respect to total bilirubin (T-BIL) and bilirubin conjugated/direct (BIL-C/D)
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End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	606	231		
Units: Subjects				
T-BIL, PRE Unknown [N=606,231]	15	4		
T-BIL, PRE Below [N=606,231]	0	0		
T-BIL, PRE Normal [N=606,231]	587	224		
T-BIL, PRE Above [N=606,231]	4	3		
T-BIL, Day 42 Unknown [N=583,220]	16	4		
T-BIL, Day 42 Below [N=583,220]	0	0		
T-BIL, Day 42 Normal [N=583,220]	558	214		
T-BIL, Day 42 Above [N=583,220]	9	2		
T-BIL, Day 182 Unknown [N=304,110]	6	0		
T-BIL, Day 182 Below [N=304,110]	0	0		
T-BIL, Day 182 Normal [N=304,110]	296	110		
T-BIL, Day 182 Above [N=304,110]	2	0		
T-BIL, Day 385 Unknown [N=251,104]	7	1		
T-BIL, Day 385 Below [N=251,104]	0	0		
T-BIL, Day 385 Normal [N=251,104]	240	102		
T-BIL, Day 385 Above [N=251,104]	4	1		
BIL-C/D, PRE Unknown [N=606,231]	15	4		
BIL-C/D, PRE Below [N=606,231]	0	0		
BIL-C/D, PRE Normal [N=606,231]	591	226		
BIL-C/D, PRE Above [N=606,231]	0	1		
BIL-C/D, Day 42 Unknown [N=583,220]	16	4		
BIL-C/D, Day 42 Below [N=583,220]	0	0		
BIL-C/D, Day 42 Normal [N=583,220]	558	214		
BIL-C/D, Day 42 Above [N=583,220]	9	2		
BIL-C/D, Day 182 Unknown [N=304,110]	7	0		
BIL-C/D, Day 182 Below [N=304,110]	0	0		
BIL-C/D, Day 182 Normal [N=304,110]	297	110		
BIL-C/D, Day 182 Above [N=304,110]	0	0		
BIL-C/D, Day 385 Unknown [N=251,104]	8	1		
BIL-C/D, Day 385 Below [N=251,104]	0	0		
BIL-C/D, Day 385 Normal [N=251,104]	240	103		
BIL-C/D, Day 385 Above [N=251,104]	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).
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End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical

investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

End point type	Secondary
End point timeframe:	
During the 21-day (Days 0-20) post-vaccination period following Dose 1 of vaccine/placebo	

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
Subject(s) with any unsolicited AEs	153	63		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).
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End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

End point type	Secondary
End point timeframe:	
During the 21-day (Days 21-41) post-vaccination period following Dose 2 of vaccine/placebo	

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	593	224		
Units: Subjects				
Subject(s) with any unsolicited AEs	135	54		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).
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End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

End point type	Secondary
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End point timeframe:

During the 42-day (Days 0-41) post-vaccination period following Dose 1 of vaccine/placebo

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
Subject(s) with any unsolicited AEs	243	97		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)
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End point description:

A SAE was defined as any untoward medical occurrence that: resulted in death, was life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
Subject(s) with any SAE(s)	8	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)
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End point description:

A SAE was defined as any untoward medical occurrence that: resulted in death, was life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

From Day U0 up to Day U385

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Subjects				
Subject(s) with any SAE(s)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).
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End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

End point type	Secondary
End point timeframe:	
During the 21-day (Days U0-U20) post-vaccination period following Dose 1 of Influenza A (H5N1) Virus monovalent vaccine	

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Subjects				
Subject(s) with any unsolicited AEs	21			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).
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End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

End point type	Secondary
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End point timeframe:

During the 21-day (Days U21-U41) post-vaccination period following Dose 2 of Influenza A (H5N1) Virus monovalent vaccine

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Subjects				
Subject(s) with any unsolicited AEs	27			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).
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End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

End point type	Secondary
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End point timeframe:

During the 42-day (Days U0-U41) post-vaccination period following Dose 1 of Influenza A (H5N1) Virus monovalent vaccine

End point values	Placebo/Influenza A (H5N1) Adjuvanted Group			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Subjects				
Subject(s) with any unsolicited AEs	41			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal biochemical parameters assessed with respect to creatinine (CREA) and blood urea nitrogen (BUN)

End point title	Number of subjects with normal and abnormal biochemical parameters assessed with respect to creatinine (CREA) and blood urea nitrogen (BUN)
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End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
CREA, PRE Unknown [N=606,231]	15	4		
CREA, PRE Below [N=606, 231]	142	61		
CREA, PRE Within [N=606, 231]	447	165		
CREA, PRE Above [N=606, 231]	2	1		
CREA, Day 42 Unknown [N=583,220]	17	4		
CREA, Day 42 Below [N=583,220]	130	48		
CREA, Day 42 Within [N=583,220]	432	166		
CREA, Day 42 Above [N=583,220]	4	2		
CREA, Day 182 Unknown [N=304,110]	6	1		
CREA, Day 182 Below [N=304,110]	66	26		
CREA, Day 182 Within [N=304,110]	231	83		
CREA, Day 182 Above [N=304,110]	1	0		
CREA, Day 385 Unknown [N=251,104]	6	0		
CREA, Day 385 Below [N=251,104]	51	24		
CREA, Day 385 Within [N=251,104]	191	80		
CREA, Day 385 Above [N=251,104]	3	0		
BUN, PRE Unknown [N=606,231]	15	4		
BUN, PRE Below [N=606,231]	13	4		
BUN, PRE Within [N=606,231]	553	218		
BUN, PRE Above [N=606,231]	25	5		
BUN, Day 42 Unknown [N=583,220]	17	4		
BUN, Day 42 Below [N=583,220]	11	3		
BUN, Day 42 Within [N=583,220]	531	209		
BUN, Day 42 Above [N=583,220]	24	4		
BUN, Day 182 Unknown [N=304,110]	6	0		
BUN, Day 182 Below [N=304,110]	8	2		
BUN, Day 182 Within [N=304,110]	281	105		
BUN, Day 182 Above [N=304,110]	9	3		
BUN, Day 385 Unknown [N=251,104]	7	0		
BUN, Day 385 Below [N=251,104]	3	2		
BUN, Day 385 Within [N=251,104]	237	100		
BUN, Day 385 Above [N=251,104]	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to basophils (BAS) and eosinophils (EOS)

End point title	Number of subjects with normal and abnormal haematological parameters assessed with respect to basophils (BAS) and eosinophils (EOS)
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End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day

385 which were normal, above normal, below the normal ranges or unknown.

End point type	Secondary
End point timeframe:	
From Day 0 up to Day 385	

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
BAS, PRE Unknown [N=606,231]	29	12		
BAS, PRE Below [N=606,231]	0	0		
BAS, PRE Within [N=606,231]	576	219		
BAS, PRE Above [N=606,231]	1	0		
BAS, Day 42 Unknown [N=583,220]	34	13		
BAS, Day 42 Below [N=583,220]	0	0		
BAS, Day 42 Within [N=583,220]	549	207		
BAS, Day 42 Above [N=583,220]	0	0		
BAS, Day 182 Unknown [N=304,110]	17	2		
BAS, Day 182 Below [N=304,110]	0	0		
BAS, Day 182 Within [N=304,110]	287	108		
BAS, Day 182 Above [N=304,110]	0	0		
BAS, Day 385 Unknown [N=251,104]	6	3		
BAS, Day 385 Below [N=251,104]	0	0		
BAS, Day 385 Within [N=251,104]	245	101		
BAS, Day 385 Above [N=251,104]	0	0		
EOS, PRE Unknown [N=606,231]	29	12		
EOS, PRE Below [N=606,231]	68	19		
EOS, PRE Within [N=606,231]	473	187		
EOS, PRE Above [N=606,231]	36	13		
EOS, Day 42 Unknown [N=583,220]	34	13		
EOS, Day 42 Below [N=583,220]	49	15		
EOS, Day 42 Within [N=583,220]	452	175		
EOS, Day 42 Above [N=583,220]	48	17		
EOS, Day 182 Unknown [N=304,110]	17	2		
EOS, Day 182 Below [N=304,110]	33	11		
EOS, Day 182 Within [N=304,110]	237	85		
EOS, Day 182 Above [N=304,110]	17	12		
EOS, Day 385 Unknown [N=251,104]	6	3		
EOS, Day 385 Below [N=251,104]	32	17		
EOS, Day 385 Within [N=251,104]	198	77		
EOS, Day 385 Above [N=251,104]	15	7		

Statistical analyses

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to haematocrit (Hcr) and haemoglobin (Hgb)

End point title	Number of subjects with normal and abnormal haematological parameters assessed with respect to haematocrit (Hcr) and haemoglobin (Hgb)
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End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
Hcr, PRE Unknown [N=606,231]	26	10		
Hcr, PRE Below [N=606,231]	53	21		
Hcr, PRE Within [N=606,231]	480	181		
Hcr, PRE Above [N=606,231]	47	19		
Hcr, Day 42 Unknown [N=583,220]	19	7		
Hcr, Day 42 Below [N=583,220]	45	13		
Hcr, Day 42 Within [N=583,220]	477	178		
Hcr, Day 42 Above [N=583,220]	42	22		
Hcr, Day 182 Unknown [N=304,110]	12	2		
Hcr, Day 182 Below [N=304,110]	38	7		
Hcr, Day 182 Within [N=304,110]	238	91		
Hcr, Day 182 Above [N=304,110]	16	10		
Hcr, Day 385 Unknown [N=251,104]	5	3		
Hcr, Day 385 Below [N=251,104]	18	12		
Hcr, Day 385 Within [N=251,104]	215	85		
Hcr, Day 385 Above [N=251,104]	13	4		
Hgb, PRE Unknown [N=606,231]	26	10		
Hgb, PRE Below [N=606,231]	61	26		
Hgb, PRE Within [N=606,231]	497	182		
Hgb, PRE Above [N=606,231]	22	13		
Hgb, Day 42 Unknown [N=583,220]	19	8		
Hgb, Day 42 Below [N=583,220]	69	19		
Hgb, Day 42 Within [N=583,220]	476	185		
Hgb, Day 42 Above [N=583,220]	19	8		
Hgb, Day 182 Unknown [N=304,110]	11	2		
Hgb, Day 182 Below [N=304,110]	42	16		
Hgb, Day 182 Within [N=304,110]	241	89		
Hgb, Day 182 Above [N=304,110]	10	3		
Hgb, Day 385 Unknown [N=251,104]	5	3		

Hbg, Day 385 Below [N=251,104]	27	15		
Hbg, Day 385 Within [N=251,104]	210	84		
Hbg, Day 385 Above [N=251,104]	9	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to neutrophils (NEU) and platelets (PLA)

End point title	Number of subjects with normal and abnormal haematological parameters assessed with respect to neutrophils (NEU) and platelets (PLA)
End point description:	
Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.	
End point type	Secondary
End point timeframe:	
From Day 0 up to Day 385	

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
NEU, PRE Unknown [N=606,231]	29	12		
NEU, PRE Below [N=606,231]	26	10		
NEU, PRE Within [N=606,231]	534	202		
NEU, PRE Above [N=606,231]	17	7		
NEU, Day 42 Unknown [N=583,220]	34	13		
NEU, Day 42 Below [N=583,220]	29	8		
NEU, Day 42 Within [N=583,220]	505	189		
NEU, Day 42 Above [N=583,220]	15	10		
NEU, Day 182 Unknown [N=304,110]	17	2		
NEU, Day 182 Below [N=304,110]	14	3		
NEU, Day 182 Within [N=304,110]	266	105		
NEU, Day 182 Above [N=304,110]	7	0		
NEU, Day 385 Unknown [N=251,104]	6	3		
NEU, Day 385 Below [N=251,104]	12	3		
NEU, Day 385 Within [N=251,104]	227	96		
NEU, Day 385 Above [N=251,104]	6	2		
PLA, PRE Unknown [N=606,231]	35	17		
PLA, PRE Below [N=606,231]	3	0		
PLA, PRE Within [N=606,231]	518	187		
PLA, PRE Above [N=606,231]	50	27		
PLA, Day 42 Unknown [N=583,220]	32	12		

PLA, Day 42 Below [N=583,220]	1	0		
PLA, Day 42 Within [N=583,220]	500	184		
PLA, Day 42 Above [N=583,220]	50	24		
PLA, Day 182 Unknown [N=304,110]	20	5		
PLA, Day 182 Below [N=304,110]	0	0		
PLA, Day 182 Within [N=304,110]	260	96		
PLA, Day 182 Above [N=304,110]	24	9		
PLA, Day 385 Unknown [N=251,104]	8	8		
PLA, Day 385 Below [N=251,104]	1	0		
PLA, Day 385 Within [N=251,104]	234	94		
PLA, Day 385 Above [N=251,104]	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to lymphocytes (LYM) and monocytes (MON)

End point title	Number of subjects with normal and abnormal haematological parameters assessed with respect to lymphocytes (LYM) and monocytes (MON)
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End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
LYM, PRE Unknown [N=606,231]	29	12		
LYM, PRE Below [N=606,231]	7	1		
LYM, PRE Within [N=606,231]	441	161		
LYM, PRE Above [N=606,231]	129	57		
LYM, Day 42 Unknown [N=583,220]	34	13		
LYM, Day 42 Below [N=583,220]	6	2		
LYM, Day 42 Within [N=583,220]	446	162		
LYM, Day 42 Above [N=583,220]	97	43		
LYM, Day 182 Unknown [N=304,110]	17	2		
LYM, Day 182 Below [N=304,110]	0	1		
LYM, Day 182 Within [N=304,110]	235	93		
LYM, Day 182 Above [N=304,110]	52	14		
LYM, Day 385 Unknown [N=251,104]	6	3		

LYM, Day 385 Below [N=251,104]	0	0		
LYM, Day 385 Within [N=251,104]	223	86		
LYM, Day 385 Above [N=251,104]	22	15		
MON, PRE Unknown [N=606,231]	29	12		
MON, PRE Below [N=606,231]	94	46		
MON, PRE Within [N=606,231]	480	170		
MON, PRE Above [N=606,231]	3	3		
MON, Day 42 Unknown [N=583,220]	34	13		
MON, Day 42 Below [N=583,220]	110	37		
MON, Day 42 Within [N=583,220]	434	167		
MON, Day 42 Above [N=583,220]	5	3		
MON, Day 182 Unknown [N=304,110]	17	2		
MON, Day 182 Below [N=304,110]	61	20		
MON, Day 182 Within [N=304,110]	221	88		
MON, Day 182 Above [N=304,110]	5	0		
MON, Day 385 Unknown [N=251,104]	6	3		
MON, Day 385 Below [N=251,104]	31	18		
MON, Day 385 Within [N=251,104]	211	83		
MON, Day 385 Above [N=251,104]	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to red and white blood cells (RBC and WBC)

End point title	Number of subjects with normal and abnormal haematological parameters assessed with respect to red and white blood cells (RBC and WBC)
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End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

End point type	Secondary
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End point timeframe:

From Day 0 up to Day 385

End point values	Influenza A (H5N1) adjuvanted Group	Placebo Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	607	231		
Units: Subjects				
RBC, PRE Unknown [N=606,231]	26	10		
RBC, PRE Below [N=606,231]	25	4		
RBC, PRE Within [N=606,231]	504	198		
RBC, PRE Above [N=606,231]	51	19		
RBC, Day 42 Unknown [N=583,220]	19	8		

RBC, Day 42 Below [N=583,220]	21	6		
RBC, Day 42 Within [N=583,220]	496	189		
RBC, Day 42 Above [N=583,220]	47	17		
RBC, Day 182 Unknown [N=304,110]	11	2		
RBC, Day 182 Below [N=304,110]	13	5		
RBC, Day 182 Within [N=304,110]	266	93		
RBC, Day 182 Above [N=304,110]	14	10		
RBC, Day 385 Unknown [N=251,104]	5	3		
RBC, Day 385 Below [N=251,104]	8	2		
RBC, Day 385 Within [N=251,104]	214	90		
RBC, Day 385 Above [N=251,104]	24	9		
WBC, PRE Unknown [N=606,231]	29	12		
WBC, PRE Below [N=606,231]	27	9		
WBC, PRE Within [N=606,231]	543	207		
WBC, PRE Above [N=606,231]	7	3		
WBC, Day 42 Unknown [N=583,220]	34	13		
WBC, Day 42 Below [N=583,220]	38	8		
WBC, Day 42 Within [N=583,220]	508	198		
WBC, Day 42 Above [N=583,220]	3	1		
WBC, Day 182 Unknown [N=304,110]	17	2		
WBC, Day 182 Below [N=304,110]	21	7		
WBC, Day 182 Within [N=304,110]	264	101		
WBC, Day 182 Above [N=304,110]	2	0		
WBC, Day 385 Unknown [N=251,104]	6	3		
WBC, Day 385 Below [N=251,104]	15	6		
WBC, Day 385 Within [N=251,104]	230	94		
WBC, Day 385 Above [N=251,104]	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for microneutralization (MN) antibodies against the H5N1 A/Indonesia virus strain.

End point title	Number of subjects seropositive for microneutralization (MN) antibodies against the H5N1 A/Indonesia virus strain.
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End point description:

End point type	Secondary
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End point timeframe:

At Days 0 and 42

End point values	Influenza A (H5N1) adjuvanted 6-<36M Group	Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group	Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group	Placebo 6-<36M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	40	7
Units: Subjects				
At Day 0	0	6	5	1
At Day 42	34	37	40	0

End point values	Placebo 3-<9Y Group	Placebo 9-<18Y Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: Subjects				
At Day 0	0	1		
At Day 42	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse events (SAE) = Day 0 to Day 385 and Day U0 to U385. Solicited local and general symptoms = During the 7-day period post vaccine/placebo administration. Unsolicited AEs = During the 42-day post vaccine/placebo administration.

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, number of participants at risk included those from Total Vaccinated cohort who had the symptom sheet completed. The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	Influenza A (H5N1) adjuvanted Group
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Reporting group description:

This group results from the pooling of the Influenza A (H5N1) adjuvanted 6-<36M, Influenza A (H5N1) adjuvanted 3-<9Y and Influenza A (H5N1) adjuvanted 9-<18Y groups and includes subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group title	Placebo Group
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Reporting group description:

This group results from the pooling of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups and includes subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who received 2 doses of 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Reporting group title	Placebo/Influenza A (H5N1) adjuvanted Group
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Reporting group description:

Subjects in this group were those who were administered the saline placebo solution in the Blinded Phase of the study (either in the Placebo 6-<36M, Placebo 3-<9Y or Placebo 9-<18Y Group). These were subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who had received 2 doses of saline placebo at Days 0 and 21 in the Blinded Phase of the study, as per described in the descriptions of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups. After consenting to participating to the Unblinded Phase of the study, these subjects received in addition 2 doses of Influenza A (H5N1) Virus monovalent vaccine at Days 385 (Day U0) and Day 385 + 21 days (Day U21). Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. Dose 1 of was administered in the deltoid region of the non-dominant arm and Dose 2 in the deltoid region of the dominant arm.

Serious adverse events	Influenza A (H5N1) adjuvanted Group	Placebo Group	Placebo/Influenza A (H5N1) adjuvanted Group
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 607 (1.32%)	4 / 231 (1.73%)	2 / 155 (1.29%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Skeletal injury	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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
Wound	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	0 / 607 (0.00%)	0 / 231 (0.00%)	1 / 155 (0.65%)
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	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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			
Lymphadenitis	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	0 / 607 (0.00%)	1 / 231 (0.43%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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

Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	0 / 607 (0.00%)	1 / 231 (0.43%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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
Psychiatric disorders			
Suicidal ideation	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	0 / 607 (0.00%)	1 / 231 (0.43%)	0 / 155 (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			
Infectious mononucleosis	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	2 / 607 (0.33%)	0 / 231 (0.00%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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
Upper respiratory tract infection	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		

subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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
Scarlet fever	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	0 / 607 (0.00%)	0 / 231 (0.00%)	1 / 155 (0.65%)
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			
Dehydration	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	1 / 607 (0.16%)	0 / 231 (0.00%)	0 / 155 (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
Type 1 diabetes mellitus	Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group.		
subjects affected / exposed	0 / 607 (0.00%)	1 / 231 (0.43%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Influenza A (H5N1) adjuvanted Group	Placebo Group	Placebo/Influenza A (H5N1) adjuvanted Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	405 / 607 (66.72%)	69 / 231 (29.87%)	111 / 155 (71.61%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	405 / 603 (67.16%)	69 / 229 (30.13%)	111 / 154 (72.08%)
occurrences (all)	405	69	111
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed ^[2]	41 / 603 (6.80%)	1 / 229 (0.44%)	5 / 154 (3.25%)
occurrences (all)	41	1	5
Drowsiness			

alternative assessment type: Systematic			
subjects affected / exposed ^[3]	101 / 294 (34.35%)	29 / 122 (23.77%)	23 / 79 (29.11%)
occurrences (all)	101	29	23
Irritability/fussiness			
alternative assessment type: Systematic			
subjects affected / exposed ^[4]	128 / 294 (43.54%)	40 / 122 (32.79%)	28 / 79 (35.44%)
occurrences (all)	128	40	28
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed ^[5]	79 / 294 (26.87%)	29 / 122 (23.77%)	18 / 79 (22.78%)
occurrences (all)	79	29	18
Fever (axillary temperature \geq 38.0°C) (children less than 6 years of age)			
alternative assessment type: Systematic			
subjects affected / exposed ^[6]	59 / 294 (20.07%)	21 / 122 (17.21%)	4 / 79 (5.06%)
occurrences (all)	59	21	4
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed ^[7]	89 / 309 (28.80%)	19 / 107 (17.76%)	18 / 75 (24.00%)
occurrences (all)	89	19	18
Gastrointestinal disorders			
alternative assessment type: Systematic			
subjects affected / exposed ^[8]	43 / 309 (13.92%)	18 / 107 (16.82%)	7 / 75 (9.33%)
occurrences (all)	42	17	7
Headache			
alternative assessment type: Systematic			
subjects affected / exposed ^[9]	100 / 309 (32.36%)	18 / 107 (16.82%)	24 / 75 (32.00%)
occurrences (all)	100	18	24
Joint pain at other location			
alternative assessment type: Systematic			
subjects affected / exposed ^[10]	50 / 309 (16.18%)	9 / 107 (8.41%)	14 / 75 (18.67%)
occurrences (all)	50	9	14
Muscle aches			
alternative assessment type: Systematic			

subjects affected / exposed ^[11]	123 / 309 (39.81%)	17 / 107 (15.89%)	34 / 75 (45.33%)
occurrences (all)	123	17	34
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed ^[12]	25 / 309 (8.09%)	7 / 107 (6.54%)	7 / 75 (9.33%)
occurrences (all)	25	7	7
Sweating			
alternative assessment type: Systematic			
subjects affected / exposed ^[13]	25 / 309 (8.09%)	4 / 107 (3.74%)	5 / 75 (6.67%)
occurrences (all)	25	4	5
Fever (axillary temperature \geq 38.0°C) (children with at least 6 years of age)			
alternative assessment type: Systematic			
subjects affected / exposed ^[14]	19 / 309 (6.15%)	3 / 107 (2.80%)	1 / 75 (1.33%)
occurrences (all)	19	3	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	13 / 607 (2.14%)	12 / 231 (5.19%)	3 / 155 (1.94%)
occurrences (all)	15	14	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	36 / 607 (5.93%)	17 / 231 (7.36%)	9 / 155 (5.81%)
occurrences (all)	36	17	9
Rhinorrhoea			
subjects affected / exposed	27 / 607 (4.45%)	13 / 231 (5.63%)	3 / 155 (1.94%)
occurrences (all)	27	13	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	29 / 607 (4.78%)	18 / 231 (7.79%)	10 / 155 (6.45%)
occurrences (all)	29	18	10

Notes:

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

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

medications, respectively).

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

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 September 2010	At the request of the U.S. Center for Biologics Research (CBER): (1) an independent data monitoring committee (IDMC) replaces the internal Safety Review Committee (iSRC) described in the previous version of the protocol, and (2) a blood sample for immunogenicity assessment has been added at the Day 21 visit. To facilitate receipt of immune-response information by participating study sites before epochs 4 and 5 begin, unblinding will occur after completion of the Day 182 visit. The language describing randomization of supplies has been modified to clarify that the vaccine will be presented in multi-dose vials that will be used as monodose vials in this study. Finally, several minor editorial errors have been corrected.
08 December 2010	The total volume of blood collected on Days 0, 42, and 182 or 385 has been decreased from 8.5 mL to 7 mL. The total volume of blood collected on Day 21 has been increased from 3.5 mL to 5 mL. These changes reflect a decrease in blood volume for safety laboratory assessments from 5 mL to 2 mL, as only a 2 mL sample is required by the central laboratory performing the tests. The total volume of blood collected for immune response assessments has been increased to 5 mL rather than 3.5 mL to allow for expanded testing for cross-reactive antibodies. Unblinding at the subject level will take place following the Day 385 analysis, as earlier unblinding potentially compromises assessment of adverse events during the interval between Days 183 and 385. A limit has been placed on the amount of time that may elapse following Day 385 during which placebo subjects may receive open-label, AS03-adjuvanted Q-PAN H5N1 vaccine. A table replaces the list of potential immune mediated diseases in Section 8.3.2.5. Minor editorial changes have also been made.
11 April 2011	Subject (family) unblinding will occur for each subject after completion of RDE, following the Day 385 contact, so the investigator can communicate treatment assignments to facilitate start of the unblinded portion of study (2nd year) for subjects who received placebo. Day U0 no longer can start on the same day as Day 385 due to the process by which unblinding at the subject level occurs. The process for allocation of subjects to a time point for the fourth blood sampling has been clarified. Assignment to a visit (and fourth blood sampling) at Day 182 and a phone call at Day 385 or the opposite will occur through an algorithm outside the randomization system and will be relayed to the investigator through the RDE system. The requirement for assessment of blood pressure during the Day 0/Screening visit physical exam has been removed, to align with clinical practice. In study procedure (Table 2), the activity "Randomization" had been inadvertently omitted and now has been added. In study procedure (Table 2), footnote # 10 was added to note that families with more than one child in the study may choose to have the follow-up phone contact for one child by interview at the time of the sibling's follow-up clinic visit (provided timings are within specified windows). To align study procedures (Table 3) with Section 5.7.3, the activity "Physical Exam" has been removed and the activity "Targeted physical exam, prn" has been added to Visit U1 (Day U0). In study procedures (Table 3), the activity "Targeted physical exam, prn" has been removed from Day U7 and Day U28 because these are telephone contacts. In Section 9.5 (Screen and baseline failures), "Influenza disease severity risk data" was removed as such data is not entered into the eCRF for this study. Edits have been made to the footnotes of study procedure (Table 2 and Table 3) for clarification purposes. The GSK Asset Number for the monovalent H5N1 vaccine was corrected. Minor editorial changes have also been made.

19 June 2012	<p>At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator will have full authority to break the treatment code.</p> <p>Clarification that unblinding at the subject level for site personnel, families, and monitors will occur after completion of RDE for all subjects, following their Day 385 contacts, rather than a batch of subjects at a time.</p> <p>In addition, a minor editorial error has been corrected.</p>
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported