Clinical trial results:
A Phase II, non-randomised, open-label study to evaluate the safety and immunogenicity of the adjuvanted (pre-) pandemic H5N1 influenza candidate vaccine following a heterologous prime-boost schedule (six months apart) in children aged 6 to 35 months.

Summary

EudraCT number	2011-004734-33
Trial protocol	Outside EU/EEA
Global end of trial date	02 November 2012

Results information

Result version number	v1
This version publication date	13 May 2016
First version publication date	24 May 2015

Trial information

Trial identification

Sponsor protocol code	109825

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01323946
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000160-PIP01-07
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	14 February 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 June 2012
Global end of trial reached?	Yes
Global end of trial date	02 November 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether a heterologous booster dose of H5N1 (A/turkey/Turkey/1/2005) haemagglutinin (HA) given 6 months following a 2-dose primary vaccination series with H5N1 (A/Indonesia/05/2005) HA elicits an antibody response that meets the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) guidance targets for pre-pandemic vaccine seroconversion rate (SCR)*, seroprotection rate (SPR)* and mean geometric increase (MGI)* based on haemagglutination inhibition (HI) responses to A/turkey/Turkey/1/2005 (H5N1) ten days following booster vaccination.

Protection of trial subjects:

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 April 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 29
Country: Number of subjects enrolled	Singapore: 84
Worldwide total number of subjects	113
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)	80
Children (2-11 years)	33
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: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK1562902A 6<12 M Group

Arm description:

Subjects between 6 and 12 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.

Arm type	Experimental
Investigational medicinal product name	GSK1562902A vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly in the anterolateral thigh

Arm title	GSK1562902A 12<24 M Group

Arm description:

Subjects between 12 and 24 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.

Arm type	Experimental
Investigational medicinal product name	GSK1562902A vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly in the deltoid region of arm

Investigational medicinal product name	GSK1562902A vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly in the deltoid region of arm

Arm title	GSK1562902A 24<36 M Group

Arm description:

Subjects between 24 and 36 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.

Arm type	Experimental
Investigational medicinal product name	GSK1562902A vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly in the deltoid region of arm

Number of subjects in period 1	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group
Started	46	34	33
Completed	43	31	33
Not completed	3	3	0
Consent withdrawn by subject	3	3	-

Baseline characteristics

Reporting groups	
Reporting group title	GSK1562902A 6<12 M Group
Reporting group description:	
Subjects between 6 and 12 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.	
Reporting group title	GSK1562902A 12<24 M Group
Reporting group description:	
Subjects between 12 and 24 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.	
Reporting group title	GSK1562902A 24<36 M Group
Reporting group description:	
Subjects between 24 and 36 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.	

Reporting group values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group
Number of subjects	46	34	33
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	8.3	16.1	29.6
standard deviation	± 1.56	± 3.44	± 3.38
Gender categorical Units: Subjects			
Female	25	19	19
Male	21	15	14

Reporting group values	Total		
Number of subjects	113		
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	63		
Male	50		

Subject analysis sets

Subject analysis set title	GSK1562902A Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.

Reporting group values	GSK1562902A Group		
Number of subjects	113		
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	16.9		
standard deviation	± 9.29		
Gender categorical			
Units: Subjects			
Female	63		
Male	50		

End points

End points reporting groups

Reporting group title	GSK1562902A 6<12 M Group
Reporting group description:	
Subjects between 6 and 12 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.	
Reporting group title	GSK1562902A 12<24 M Group
Reporting group description:	
Subjects between 12 and 24 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.	
Reporting group title	GSK1562902A 24<36 M Group
Reporting group description:	
Subjects between 24 and 36 months of age, who received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.	
Subject analysis set title	GSK1562902A Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received 2 primary doses of A/Indonesia/05/2005 H5N1 vaccine on Days 0 and 21 and 1 booster dose of the A/turkey/Turkey/1/2005 H5N1 vaccine on Day 182.	

Primary: Number of seroconverted subjects in terms of HI antibodies

End point title	Number of seroconverted subjects in terms of HI antibodies[1]
End point description:	
HI antibody concentration against A/turkey/Turkey/01/2005	
End point type	Primary
End point timeframe:	
At Day 192	
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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.	

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Subjects				
A/turkey/Turkey/01/2005.HA [Day 192]	83			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric mean of the within-subject ratios

End point title	Geometric mean of the within-subject ratios[2]
End point description:	
HI antibody concentration against Flu A/Turk/01/05 (H5N1)	

End point type	Primary

End point timeframe:

At Day 192

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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Turk/01/05 (H5N1).HA [Day 192]	357.7 (302.4 to 423.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for HI antibodies

End point title	Number of seroprotected subjects for HI antibodies[3]

End point description:

HI antibody concentration against A/turkey/Turkey/01/2005

End point type	Primary

End point timeframe:

At Day 192

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Subjects				
A/turkey/Turkey/01/2005.HA [Day192]	83			

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titers

End point title	HI antibody titers

End point description:

HI antibody concentration against A/Indonezia/05/2005

End point type	Secondary

End point timeframe:

At Day 0, Day 42, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Titers				
geometric mean (confidence interval 95%)				
A/Indonesia/05/2005.HA [Day 0]	5 (5 to 5)			
A/Indonesia/05/2005.HA [Day 42]	1078.6 (935.3 to 1243.7)			
A/Indonesia/05/2005.HA [Day 182]	147.2 (129.6 to 167.1)			
A/Indonesia/05/2005.HA [Day 192]	1787.6 (1552.4 to 2058.3)			
A/Indonesia/05/2005.HA [Day 364]	1043.3 (886.1 to 1228.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titers

End point title	HI antibody titers

End point description:

HI antibody concentration against A/turkey/Turkey/01/2005

End point type	Secondary

End point timeframe:

At Day 0, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Titers				
geometric mean (confidence interval 95%)				
A/turkey/Turkey/01/2005.HA [Day 0]	5.7 (5.2 to 6.2)			
A/turkey/Turkey/01/2005.HA [Day 182]	89.3 (79.1 to 100.7)			
A/turkey/Turkey/01/2005.HA [Day 192]	2026.2 (1731.3 to 2371.3)			

A/turkey/Turkey/01/2005.HA [Day 364]	1266.8 (1080.6 to 1485)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-HIs antibody concentrations ≥ 1:10

End point title	Number of subjects with anti-HIs antibody concentrations ≥ 1:10

End point description:

HI antibody concentration against A/Indonezia/05/2005

End point type	Secondary

End point timeframe:

At Day 0, Day 42, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Subjects				
A/Indonesia/05/2005.HA [Day 0]	0			
A/Indonesia/05/2005.HA [Day 42]	85			
A/Indonesia/05/2005.HA [Day 182]	83			
A/Indonesia/05/2005.HA [Day 192]	83			
A/Indonesia/05/2005.HA [Day 364]	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-HIs antibody concentrations ≥ 1:10

End point title	Number of subjects with anti-HIs antibody concentrations ≥ 1:10

End point description:

HI antibody concentration against A/turkey/Turkey/01/2005

End point type	Secondary

End point timeframe:

At Day 0, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Subjects				
A/turkey/Turkey/01/2005.HA [Day 0]	11			
A/turkey/Turkey/01/2005.HA [Day 182]	83			
A/turkey/Turkey/01/2005.HA [Day 192]	83			
A/turkey/Turkey/01/2005.HA [Day 364]	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects in terms of HI antibodies

End point title	Number of seroconverted subjects in terms of HI antibodies
End point description:	
HI antibody concentration against A/Indonezia/05/2005	
End point type	Secondary
End point timeframe:	
At Day 42, Day 182, Day 192 and Day 364	

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Subjects				
A/Indonesia/05/2005.HA [Day 42]	85			
A/Indonesia/05/2005.HA [Day 182]	83			
A/Indonesia/05/2005.HA [Day 192]	83			
A/Indonesia/05/2005.HA [Day 364]	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects in terms of HI antibodies

End point title	Number of seroconverted subjects in terms of HI antibodies
End point description:	
HI antibody concentration against Flu A/Turk/01/05 (H5N1)	
End point type	Secondary
End point timeframe:	
At Day 364	

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: Subjects				
Flu A/Turk/01/05 (H5N1).HA [Day 364]	95			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for HI antibodies

End point title	Number of seroprotected subjects for HI antibodies

End point description:

End point type	Secondary

End point timeframe:

At Day 0 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Subjects				
Flu A/Ind/05/05 (H5N1).HA [Day 0]	0			
Flu A/Ind/05/05 (H5N1).HA [Day 364]	100			
Flu A/Turk/01/05 (H5N1).HA [Day 0]	1			
Flu A/Turk/01/05 (H5N1).HA [Day 364]	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean of the within-subject ratios for the assessed H5N1 strains

End point title	Geometric mean of the within-subject ratios for the assessed H5N1 strains

End point description:

End point type	Secondary

End point timeframe:

At Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Ind/05/05 (H5N1).HA [Day 364]	208.7 (177.2 to 245.7)			
Flu A/Turk/01/05 (H5N1).HA [Day 364]	14.9 (12.6 to 17.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects in terms of HI antibodies

End point title	Number of seroconverted subjects in terms of HI antibodies

End point description:

HI antibody concentration against A/turkey/Turkey/01/2005.HA

End point type	Secondary

End point timeframe:

At Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: Subjects				
A/turkey/Turkey/01/2005.HA [Day 192]	82			
A/turkey/Turkey/01/2005.HA [Day 364]	95			

Statistical analyses

No statistical analyses for this end point

Secondary: Booster Factor

End point title	Booster Factor

End point description:

Booster Factor was defined as the geometric mean of the within-subject ratios of the post-booster

vaccination reciprocal HI titre to the pre-booster (Day 182) reciprocal titre.

End point type	Secondary

End point timeframe:

At Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: Titers				
geometric mean (confidence interval 95%)				
A/turkey/Turkey/01/2005.HA [Day 192]	22.7 (19.3 to 26.8)			
A/turkey/Turkey/01/2005.HA [Day 364]	14.9 (12.6 to 17.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serum neutralising antibody titers ≥ 1:28

End point title	Number of subjects with serum neutralising antibody titers ≥ 1:28

End point description:

HI antibody concentration against Flu A/Ind/05/05 (H5N1)

End point type	Secondary

End point timeframe:

Day 0, Day 42, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	95			
Units: Subjects				
Flu A/Ind/05/05 (H5N1) [Day 0]	1			
Flu A/Ind/05/05 (H5N1) [Day 42]	70			
Flu A/Ind/05/05 (H5N1) [Day 182]	81			
Flu A/Ind/05/05 (H5N1) [Day 192]	83			
Flu A/Ind/05/05 (H5N1) [Day 364]	95			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serum neutralising antibody titers ≥ 1:28

End point title	Number of subjects with serum neutralising antibody titers ≥ 1:28

End point description:

HI antibody concentration against Flu A/Turk/01/05 (H5N1)

End point type	Secondary

End point timeframe:

Day 0, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	95			
Units: Subjects				
Flu A/Turk/01/05 (H5N1) [Day 0]	0			
Flu A/Turk/01/05 (H5N1) [Day 182]	81			
Flu A/Turk/01/05 (H5N1) [Day 192]	83			
Flu A/Turk/01/05 (H5N1) [Day 364]	95			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum neutralising antibody titres

End point title	Serum neutralising antibody titres

End point description:

Antibody titers against Flu A/Ind/05/05 (H5N1)

End point type	Secondary

End point timeframe:

Day 0, Day 42, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	95			
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Ind/05/05 (H5N1) [Day 0]	14.1 (13.9 to 14.4)			
Flu A/Ind/05/05 (H5N1) [Day 42]	1858 (1491.3 to 2315)			

Flu A/Ind/05/05 (H5N1) [Day 182]	448.7 (379 to 531.2)			
Flu A/Ind/05/05 (H5N1) [Day 192]	11215.7 (9797.4 to 12839.2)			
Flu A/Ind/05/05 (H5N1) [Day 364]	4283.3 (3485.8 to 5263.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum neutralising antibody titres

End point title	Serum neutralising antibody titres

End point description:

HI antibody concentration against Flu A/Turk/01/05 (H5N1)

End point type	Secondary

End point timeframe:

Day 0, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	95			
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Turk/01/05 (H5N1) [Day 0]	14 (14 to 14)			
Flu A/Turk/01/05 (H5N1) [Day 182]	125.4 (111.6 to 140.8)			
Flu A/Turk/01/05 (H5N1) [Day 192]	5192.9 (4101.3 to 6575.1)			
Flu A/Turk/01/05 (H5N1) [Day 364]	2610.2 (2085.3 to 3267.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine response rate for neutralising antibodies

End point title	Vaccine response rate for neutralising antibodies

End point description:

Vaccine response rate against Flu A/Ind/05/05 (H5N1)

End point type	Secondary

End point timeframe:

At Day 42, Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Subjects				
Flu A/Ind/05/05 (H5N1) [Day 42]	62			
Flu A/Ind/05/05 (H5N1) [Day 182]	69			
Flu A/Ind/05/05 (H5N1) [Day 192]	72			
Flu A/Ind/05/05 (H5N1) [Day 364]	83			

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine response rate for neutralising antibodies

End point title	Vaccine response rate for neutralising antibodies

End point description:

Vaccine response rate against Flu A/Turk/01/05 (H5N1)

End point type	Secondary

End point timeframe:

At Day 182, Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	83			
Units: Subjects				
Flu A/Turk/01/05 (H5N1) Ab [Day 182]	58			
Flu A/Turk/01/05 (H5N1) Ab [Day 192]	72			
Flu A/Turk/01/05 (H5N1) Ab [Day 364]	83			

Statistical analyses

No statistical analyses for this end point

Secondary: Booster vaccine response for neutralising antibodies

End point title	Booster vaccine response for neutralising antibodies

End point description:

Booster vaccine response against Flu A/Turk/01/05 (H5N1)

End point type	Secondary

End point timeframe:

At Day 192 and Day 364

End point values	GSK1562902A Group			
Subject group type	Subject analysis set			
Number of subjects analysed	79			
Units: Subjects				
Flu A/Turk/01/05 (H5N1) [Day 192]	69			
Flu A/Turk/01/05 (H5N1) [Day 364]	76			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms

End point title	Number of subjects with any and Grade 3 solicited local symptoms

End point description:

End point type	Secondary

End point timeframe:

During a 7-day follow-up period, i.e. day of vaccination and 6 subsequent days after each vaccination on Day 0, Day 21 and Day 182

End point values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group	GSK1562902A Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	33	33	112
Units: Subjects				
Any Pain Dose 1	14	5	13	32
Grade 3 Pain Dose 1	2	0	1	3
Any Redness Dose 1	2	0	2	4
Grade 3 Redness Dose 1	0	0	0	0
Any Swelling Dose 1	1	1	1	3
Grade 3 Swelling Dose 1	0	0	0	0
Any Pain Dose 2	10	13	14	37
Grade 3 Pain Dose 2	0	0	1	1
Any Redness Dose 2	3	2	1	6
Grade 3 Redness Dose 2	0	0	0	0
Any Swelling Dose 2	2	2	0	4
Grade 3 Swelling Dose 2	0	0	0	0
Any Pain Dose 3	20	15	18	53

Grade 3 Pain Dose 3	3	1	3	7
Any Redness Dose 3	11	5	2	18
Grade 3 Redness Dose 3	0	0	0	0
Any Swelling Dose 3	5	5	1	11
Grade 3 Swelling Dose 3	0	0	0	0
Any Pain Across doses	26	19	21	66
Grade 3 Pain Across doses	4	1	5	10
Any Redness Across doses	13	6	3	22
Grade 3 Redness Across doses	0	0	0	0
Any Swelling Across doses	6	6	1	13
Grade 3 Swelling Across doses	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related solicited general symptoms

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms

End point description:

End point type	Secondary

End point timeframe:

During a 7-day follow-up period, i.e. day of vaccination and 6 subsequent days after each vaccination on Day 0, Day 21 and Day 182

End point values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group	GSK1562902A Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	33	33	112
Units: Subjects				
Any Diarrhoea/vomiting Dose 1	10	6	3	19
Grade 3 Diarrhoea/vomiting Dose 1	1	1	0	2
Related Diarrhoea/vomiting Dose 1	6	1	2	9
Any Drowsiness Dose 1	10	9	5	24
Grade 3 Drowsiness Dose 1	1	0	0	1
Related Drowsiness Dose 1	8	7	5	20
Any Irritability/fussiness Dose 1	21	14	9	44
Grade 3 Irritability/fussiness Dose 1	3	0	0	3
Related Irritability/fussiness Dose 1	19	10	8	37
Any Loss of appetite Dose 1	9	12	6	27
Grade 3 Loss of appetite Dose 1	0	1	0	1
Related Loss of appetite Dose 1	5	8	5	18
Any Fever (Axillary) Dose 1	4	6	4	14
Grade 3 Fever (Axillary) Dose 1	0	2	0	2
Related Fever (Axillary) Dose 1	3	5	3	11

Any Diarrhoea/vomiting Dose 2	8	3	2	13
Grade 3 Diarrhoea/vomiting Dose 2	0	0	0	0
Related Diarrhoea/vomiting Dose 2	7	2	1	10
Any Drowsiness Dose 2	8	12	7	27
Grade 3 Drowsiness Dose 2	1	1	1	3
Related Drowsiness Dose 2	8	10	7	25
Any Irritability/fussiness Dose 2	14	17	10	41
Grade 3 Irritability/fussiness Dose 2	1	3	0	4
Related Irritability/fussiness Dose 2	13	15	10	38
Any Loss of appetite Dose 2	8	6	9	23
Grade 3 Loss of appetite Dose 2	0	1	0	1
Related Loss of appetite Dose 2	8	5	8	21
Any Fever (Axillary) Dose 2	14	12	10	36
Grade 3 Fever (Axillary) Dose 2	2	3	1	6
Related Fever (Axillary) Dose 2	14	12	10	36
Any Diarrhoea/vomiting Dose 3	10	3	3	16
Grade 3 Diarrhoea/vomiting Dose 3	1	0	0	1
Related Diarrhoea/vomiting Dose 3	9	2	1	12
Any Drowsiness Dose 3	16	6	10	32
Grade 3 Drowsiness Dose 3	2	0	1	3
Related Drowsiness Dose 3	16	6	7	29
Any Irritability/fussiness Dose 3	28	15	11	54
Grade 3 Irritability/fussiness Dose 3	7	0	2	9
Related Irritability/fussiness Dose 3	26	15	10	51
Any Loss of appetite Dose 3	16	12	9	37
Grade 3 Loss of appetite Dose 3	2	0	2	4
Related Loss of appetite Dose 3	15	12	7	34
Any Fever (Axillary) Dose 3	20	15	19	54
Grade 3 Fever (Axillary) Dose 3	3	5	3	11
Related Fever (Axillary) Dose 3	19	15	18	52
Any Diarrhoea/vomiting Across doses	17	11	7	35
Grade 3 Diarrhoea/vomiting Across doses	1	1	0	2
Related Diarrhoea/vomiting Across doses	14	5	3	22
Any Drowsiness Across doses	22	18	12	52
Grade 3 Drowsiness Across doses	3	1	2	6
Related Drowsiness Across doses	21	17	12	50
Any Irritability/fussiness Across doses	35	23	15	73
Grade 3 Irritability/fussiness Across doses	10	3	2	15
Related Irritability/fussiness Across doses	35	23	14	72
Any Loss of appetite Across doses	22	18	14	54
Grade 3 Loss of appetite Across doses	2	2	2	6
Related Loss of appetite Across doses	19	17	14	50
Any Fever (Axillary) Across doses	29	19	21	69
Grade 3 Fever (Axillary) Across doses	5	8	4	17
Related Fever (Axillary) Across doses	28	19	20	67

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

During the entire study period

End point values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group	GSK1562902A Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	34	33	113
Units: Subjects				
Any MAE(s)	29	19	20	68

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune-mediated disease (pIMDs)

End point title	Number of subjects with potential immune-mediated disease (pIMDs)

End point description:

End point type	Secondary

End point timeframe:

During the entire study period

End point values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group	GSK1562902A Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	34	33	113
Units: Subjects				
Any pIMDs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

During a 21 day follow-up period after each vaccination

End point values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group	GSK1562902A Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	34	33	113
Units: Subjects				
Any AE(s)	29	19	24	72
Grade 3 AE(s)	5	3	2	10
Related AE(s)	13	5	7	25

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

Up to Day 84 follow-up period after each vaccination

End point values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group	GSK1562902A Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	34	33	113
Units: Subjects				
Any AE(s)	32	23	22	77
Grade 3 AE(s)	4	4	2	10
Related AE(s)	9	3	6	18

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

End point type	Secondary

End point timeframe:

During the entire study period

End point values	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group	GSK1562902A Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	46	34	33	113
Units: Subjects				
SAEs	5	4	0	9

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	GSK1562902A 6<12 M Group
Reporting group description: -	
Reporting group title	GSK1562902A 12<24 M Group
Reporting group description: -	
Reporting group title	GSK1562902A 24<36 M Group
Reporting group description: -	

Serious adverse events	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 46 (10.87%)	4 / 34 (11.76%)	0 / 33 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 46 (0.00%)	1 / 34 (2.94%)	0 / 33 (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			
Diarrhoea			
subjects affected / exposed	0 / 46 (0.00%)	1 / 34 (2.94%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 46 (4.35%)	0 / 34 (0.00%)	0 / 33 (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

Wheezing			
subjects affected / exposed	1 / 46 (2.17%)	0 / 34 (0.00%)	0 / 33 (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
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 46 (2.17%)	2 / 34 (5.88%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 46 (2.17%)	1 / 34 (2.94%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis viral			
subjects affected / exposed	0 / 46 (0.00%)	1 / 34 (2.94%)	0 / 33 (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
Gastroenteritis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 34 (2.94%)	0 / 33 (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
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 46 (2.17%)	0 / 34 (0.00%)	0 / 33 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 46 (0.00%)	1 / 34 (2.94%)	0 / 33 (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
Lobar pneumonia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 34 (2.94%)	0 / 33 (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
Pneumonia			

subjects affected / exposed	1 / 46 (2.17%)	0 / 34 (0.00%)	0 / 33 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 46 (0.00%)	2 / 34 (5.88%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	GSK1562902A 6<12 M Group	GSK1562902A 12<24 M Group	GSK1562902A 24<36 M Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 46 (76.09%)	23 / 34 (67.65%)	24 / 33 (72.73%)
Investigations			
Body temperature increased (Day 0-20 following vaccination)			
subjects affected / exposed	1 / 46 (2.17%)	1 / 34 (2.94%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	26 / 46 (56.52%)	19 / 33 (57.58%)	21 / 33 (63.64%)
occurrences (all)	26	19	21
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	13 / 46 (28.26%)	6 / 33 (18.18%)	3 / 33 (9.09%)
occurrences (all)	13	6	3
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	6 / 46 (13.04%)	6 / 33 (18.18%)	1 / 33 (3.03%)
occurrences (all)	6	6	1
Diarrhoea/vomiting			
alternative assessment type: Systematic			

subjects affected / exposed[4]	17 / 46 (36.96%)	11 / 33 (33.33%)	7 / 33 (21.21%)
occurrences (all)	17	11	7
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[5]	22 / 46 (47.83%)	18 / 33 (54.55%)	12 / 33 (36.36%)
occurrences (all)	22	18	12
Irritability/fussiness			
alternative assessment type: Systematic			
subjects affected / exposed[6]	35 / 46 (76.09%)	23 / 33 (69.70%)	15 / 33 (45.45%)
occurrences (all)	35	23	15
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	22 / 46 (47.83%)	18 / 33 (54.55%)	14 / 33 (42.42%)
occurrences (all)	22	18	14
Fever (Axillary)			
alternative assessment type: Systematic			
subjects affected / exposed[8]	29 / 46 (63.04%)	19 / 33 (57.58%)	21 / 33 (63.64%)
occurrences (all)	29	19	21
Pyrexia (Day 0-20 following vaccination)			
subjects affected / exposed	3 / 46 (6.52%)	3 / 34 (8.82%)	5 / 33 (15.15%)
occurrences (all)	3	3	5
Pyrexia (Day 0-84 following vaccination)			
subjects affected / exposed	6 / 46 (13.04%)	4 / 34 (11.76%)	4 / 33 (12.12%)
occurrences (all)	6	4	4
Gastrointestinal disorders			
Vomiting (Day 0-20 following vaccination)			
subjects affected / exposed	0 / 46 (0.00%)	2 / 34 (5.88%)	4 / 33 (12.12%)
occurrences (all)	0	2	4
Teething (Day 0-20 following vaccination)			
subjects affected / exposed	4 / 46 (8.70%)	1 / 34 (2.94%)	0 / 33 (0.00%)
occurrences (all)	4	1	0
Diarrhoea (Day 0-20 following vaccination)			

subjects affected / exposed	0 / 46 (0.00%)	1 / 34 (2.94%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
Vomiting (Day 0-84 following vaccination)			
subjects affected / exposed	2 / 46 (4.35%)	3 / 34 (8.82%)	1 / 33 (3.03%)
occurrences (all)	2	3	1
Teething (Day 0-84 following vaccination)			
subjects affected / exposed	4 / 46 (8.70%)	1 / 34 (2.94%)	0 / 33 (0.00%)
occurrences (all)	4	1	0
Respiratory, thoracic and mediastinal disorders			
Cough (Day 0-20 following vaccination)			
subjects affected / exposed	8 / 46 (17.39%)	5 / 34 (14.71%)	2 / 33 (6.06%)
occurrences (all)	8	5	2
Rhinorrhoea (Day 0-20 following vaccination)			
subjects affected / exposed	10 / 46 (21.74%)	2 / 34 (5.88%)	2 / 33 (6.06%)
occurrences (all)	10	2	2
Wheezing (Day 0-20 following vaccination)			
subjects affected / exposed	0 / 46 (0.00%)	2 / 34 (5.88%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Cough (Day 0-84 following vaccination)			
subjects affected / exposed	7 / 46 (15.22%)	6 / 34 (17.65%)	2 / 33 (6.06%)
occurrences (all)	7	6	2
Rhinorrhoea (Day 0-84 following vaccination)			
subjects affected / exposed	6 / 46 (13.04%)	1 / 34 (2.94%)	2 / 33 (6.06%)
occurrences (all)	6	1	2
Skin and subcutaneous tissue disorders			
Urticaria (Day 0-20 following vaccination)			
subjects affected / exposed	0 / 46 (0.00%)	0 / 34 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
Dermatitis diaper (Day 0-20 following vaccination)			
subjects affected / exposed	0 / 46 (0.00%)	2 / 34 (5.88%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Eczema (Day 0-20 following			

vaccination)			
subjects affected / exposed	0 / 46 (0.00%)	2 / 34 (5.88%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Rash (Day 0-20 following vaccination)			
subjects affected / exposed	3 / 46 (6.52%)	0 / 34 (0.00%)	1 / 33 (3.03%)
occurrences (all)	3	0	1
Dermatitis diaper (Day 0-84 following vaccination)			
subjects affected / exposed	0 / 46 (0.00%)	3 / 34 (8.82%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
Eczema (Day 0-84 following vaccination)			
subjects affected / exposed	1 / 46 (2.17%)	3 / 34 (8.82%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
Infections and infestations			
Upper respiratory tract infection (Day 0-20 following vaccination)			
subjects affected / exposed	7 / 46 (15.22%)	5 / 34 (14.71%)	11 / 33 (33.33%)
occurrences (all)	7	5	11
Nasopharyngitis (Day 0-20 following vaccination)			
subjects affected / exposed	2 / 46 (4.35%)	4 / 34 (11.76%)	2 / 33 (6.06%)
occurrences (all)	2	4	2
Rhinitis (Day 0-20 following vaccination)			
subjects affected / exposed	4 / 46 (8.70%)	0 / 34 (0.00%)	2 / 33 (6.06%)
occurrences (all)	4	0	2
Upper respiratory tract infection (Day 0-84 following vaccination)			
subjects affected / exposed	9 / 46 (19.57%)	4 / 34 (11.76%)	11 / 33 (33.33%)
occurrences (all)	9	4	11
Nasopharyngitis (Day 0-84 following vaccination)			
subjects affected / exposed	2 / 46 (4.35%)	5 / 34 (14.71%)	2 / 33 (6.06%)
occurrences (all)	2	5	2
Rhinitis (Day 0-84 following vaccination)			
subjects affected / exposed	5 / 46 (10.87%)	1 / 34 (2.94%)	2 / 33 (6.06%)
occurrences (all)	5	1	2

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 the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

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

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 January 2011	Amendment 1 The former version of the protocol was published in two versions, due to a tehnical problem. The first version contained errors in the tables of intensity (Table 15). This version was submitted in Singapore. The second version contained errors in the vaccine tables (Tables 7 and 10), where commas where left out in the volumes. This version was submitted in Australia. This Amendment is based on the latter version of the final protocol. Therefore, track changes on Table 15 will not be found in the amendment, although a difference exists with the version submitted in Singapore. The changes have been brought to the tables as explained under Section 8.2.2.2.1. Additional changes have been brought to clarify the contents of the vials and vaccine doses.
16 June 2011	Amendment 2 The protocol was amended to exclude subjects who had a past medical history of infection with a H5N1 virus or vaccination with a H5N1 vaccine. Exclusion criteria were updated accordingly. In addition, procedures for collection of medically-attended adverse events between Day 203 and Day 364 have been clarified.
04 November 2011	Amendment 3 With Amendment 3, the protocol was adjusted to document that the age stratification ratio of 2:1:1 for children 6 to 11 months, 12 to 23 months, and 24 to 35 months of age, respectively, will not be maintained due to recruitment difficulties. The overall subjects enrolment goal will not change.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported