Clinical trial results:
A phase II, randomized, observer blind study to evaluate the safety and immunogenicity of three different vaccination schedules employing two formulations of the monovalent A/California/7/2009 (H1N1)v-like candidate vaccine adjuvanted with AS03 and the monovalent A/California/7/2009 (H1N1)v-like candidate vaccine formulated without adjuvant in subjects aged 10 to less than 18 years.

Summary

EudraCT number	2009-016268-35
Trial protocol	SK EE
Global end of trial date	10 May 2011

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	06 May 2015

Trial information

Trial identification

Sponsor protocol code	113883

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01035749
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 Trials Call Centre, GlaxoSmithKline Biologicals', 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Centre, GlaxoSmithKline Biologicals', 044 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	10 May 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 May 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether vaccination with monovalent A/California/7/2009 (H1N1)v-like vaccine (each treatment group) results in an immune response to the vaccine-homologous virus that meets or exceeds the CHMP guidance targets for pandemic vaccine seroconversion rate (SCR), rate of induction of vaccine-homologous reciprocal hemagglutination inhibition (HI) titers greater than or equal to 40 (potential seroprotection rate [SPR]) and geometric mean fold rise (GMFR) 21 days after the first dose of H1N1 vaccine in children 10 to < 18 years of age.

Protection of trial subjects:

All subjects were supervised for atleast 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 182 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 2010
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	Slovakia: 110
Country: Number of subjects enrolled	Estonia: 200
Worldwide total number of subjects	310
EEA total number of subjects	310

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)	0
Children (2-11 years)	110

Adolescents (12-17 years)	200
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:

310 subjects were enrolled in the study, all of which were vaccinated and completed the Day 42 visit.

Period 1

Period 1 title	At Day 42 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Monitor, Data analyst, Carer, Assessor, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Flu1-F1-2D Group

Arm description:

Subjects received 2 doses of Arepanrix ™ formulation 1 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.

Arm type	Experimental
Investigational medicinal product name	Arepanrix™
Investigational medicinal product code	
Other name	GSK2340274A
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered intramuscularly

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:

1 dose administered intramuscularly in subjects of Flu1-F1-2D Group, Flu1-F2-2D Group and Flu2-2D Group respectively at Day 21.

Arm title	Flu1-F2-2D Group

Arm description:

Subjects received 2 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.

Arm type	Experimental
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:

1 dose administered intramuscularly in subjects of Flu1-F1-2D Group, Flu1-F2-2D Group and Flu2-2D Group respectively at Day 21.

Arm title	Flu1-F2-3D Group

Arm description:	
Subjects received 3 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0, Day 21 and Day 182 (booster).	
Arm type	Experimental
Investigational medicinal product name	Arepanrix™
Investigational medicinal product code	
Other name	Adjuvanted A/California/7/2009 (H1N1)v-like inactivated split virion
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses administered intramuscularly at Days 0, 21 and 182 (booster).	
Arm title	Flu2-2D Group
Arm description:	
Subjects received 2 doses of Arepanrix ™ unadjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.	
Arm type	Active comparator
Investigational medicinal product name	Unadjuvanted Q-Pan H1N1 vaccine
Investigational medicinal product code	
Other name	unadjuvanted A/California/7/2009 (H1N1) v-like inactivated split virion
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 doses administered intramuscularly at Days 0 and 182.	
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:	
1 dose administered intramuscularly at Day 21.	

Number of subjects in period 1	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group
Started	66	66	68
Completed	66	66	68

Number of subjects in period 1	Flu2-2D Group
Started	110
Completed	110

Baseline characteristics

Reporting groups	
Reporting group title	Flu1-F1-2D Group
Reporting group description:	
Subjects received 2 doses of Arepanrix ™ formulation 1 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.	
Reporting group title	Flu1-F2-2D Group
Reporting group description:	
Subjects received 2 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.	
Reporting group title	Flu1-F2-3D Group
Reporting group description:	
Subjects received 3 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0, Day 21 and Day 182 (booster).	
Reporting group title	Flu2-2D Group
Reporting group description:	
Subjects received 2 doses of Arepanrix ™ unadjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.	

Reporting group values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group
Number of subjects	66	66	68
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	13.6	14.5	14.6
standard deviation	± 2.27	± 2.2	± 1.84
Gender categorical			
Units: Subjects			
Female	37	32	38
Male	29	34	30

Reporting group values	Flu2-2D Group	Total	
Number of subjects	110	310	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	14.1		
standard deviation	± 2.13	-	
Gender categorical			
Units: Subjects			
Female	59	166	
Male	51	144	

End points

End points reporting groups

Reporting group title	Flu1-F1-2D Group
Reporting group description:	
Subjects received 2 doses of Arepanrix ™ formulation 1 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.	
Reporting group title	Flu1-F2-2D Group
Reporting group description:	
Subjects received 2 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.	
Reporting group title	Flu1-F2-3D Group
Reporting group description:	
Subjects received 3 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0, Day 21 and Day 182 (booster).	
Reporting group title	Flu2-2D Group
Reporting group description:	
Subjects received 2 doses of Arepanrix ™ unadjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.	

Primary: Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain[1]
End point description:	
Seroconversion defined as: - For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination - For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre	
End point type	Primary
End point timeframe:	
At Day 21	

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	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	68	109
Units: Subjects	63	58	61	96

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Seroprotected for HI Antibodies against Flu

A/CAL/7/09 H1N1 strain

End point title	Number of Subjects Seroprotected for HI Antibodies against Flu A/CAL/7/09 H1N1 strain[2]

End point description:

A seroprotected subject was defined as a subject with a serum HI titer greater than or equal to 1:40 that usually is accepted as indicating protection.

End point type	Primary

End point timeframe:

At Day 0 and Day 21

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	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	68	109
Units: Subjects				
Day 0	28	35	30	49
Day 21	66	65	67	107

Statistical analyses

No statistical analyses for this end point

Primary: HI antibody seroconversion factors against Flu A/CAL/7/09 H1N1 strain

End point title	HI antibody seroconversion factors against Flu A/CAL/7/09 H1N1 strain[3]

End point description:

Seroconversion factors were defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.

End point type	Primary

End point timeframe:

At Day 21

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

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	68	109
Units: Fold increase				
geometric mean (confidence interval 95%)	35.6 (26.4 to 47.9)	18.3 (13.1 to 25.6)	28.9 (20.4 to 41)	25.3 (19.2 to 33.3)

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point title	HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point description:

Antibody titers were expressed as GMTs.

End point type	Secondary

End point timeframe:

At Day 0 and Day 21

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	65	68	109
Units: Titre				
geometric mean (confidence interval 95%)				
Day 0	24.1 (17.2 to 33.8)	33 (22.4 to 48.7)	23.4 (16.9 to 32.4)	22.8 (17.4 to 29.9)
Day 21	858.7 (714.5 to 1032)	603.6 (493.3 to 738.5)	676.9 (539.1 to 850)	578.1 (466.7 to 716.1)

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point title	HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point description:

Antibody titres were expressed as Geometric mean titers (GMTs).

End point type	Secondary

End point timeframe:

At Day 0 and Day 42

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	65	68	108
Units: Titres				
geometric mean (confidence interval 95%)				
Day 0	23.4 (16.7 to 32.9)	33 (22.4 to 48.7)	23.4 (16.9 to 32.4)	22.7 (17.3 to 29.8)

Day 42	646.9 (532.3 to 786.2)	469.7 (386.9 to 570.3)	977 (833.1 to 1145.8)	439.6 (356 to 543)

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point title	HI antibody titres against Flu A/CAL/7/09 H1N1 strain
End point description:	
Antibody titres were expressed as GMTs.	
End point type	Secondary
End point timeframe:	
At Day 0 and Day 182	

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	65	68	109
Units: Titres				
geometric mean (confidence interval 95%)				
Day 0	22.9 (16.3 to 32)	34.8 (23.5 to 51.5)	23.4 (16.9 to 32.4)	22.8 (17.4 to 29.9)
Day 182	240.2 (188.1 to 306.6)	176.1 (137.1 to 226)	318.4 (257.8 to 393.1)	177.2 (140.1 to 224)

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point title	HI antibody titres against Flu A/CAL/7/09 H1N1 strain
End point description:	
Antibody titres were expressed as Geometric mean titers (GMTs).	
End point type	Secondary
End point timeframe:	
At Days 0, 182 and 189	

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	68	108
Units: Titres				
geometric mean (confidence interval 95%)				
Day 0	23.4 (16.7 to 32.9)	33.5 (22.5 to 50.1)	23.4 (16.9 to 32.4)	22.5 (17.2 to 29.5)
Day 182	237.7 (185.7 to 304.5)	172.7 (133.7 to 223.2)	318.4 (257.8 to 393.1)	177.3 (140 to 224.7)
Day 189	589.4 (506 to 686.5)	416.7 (352.8 to 492.2)	552.1 (474.5 to 642.5)	273.4 (233.2 to 320.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point description:

A seroconverted subject was defined as a subject who had either a pre-vaccination titre below 1:10 and a post-vaccination titre greater than or equal to 1:40 or a pre-vaccination titre greater than or equal to 1:10 and at least a 4-fold increase in post-vaccination titre.

End point type	Secondary

End point timeframe:

At Day 42

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	65	68	108
Units: Subjects	62	52	65	93

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point description:

A seroconverted subject was defined as a subject who had either a pre-vaccination titre below 1:10 and a post-vaccination titre greater than or equal to 1:40 or a pre-vaccination titre greater than or equal to 1:10 and at least a 4-fold increase in post-vaccination titre.

End point type	Secondary

End point timeframe:

At Day 182

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	65	68	109
Units: Subjects	48	34	56	67

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point description:

A seroconverted subject was defined as a subject who had either a pre-vaccination titre below 1:10 and a post-vaccination titre greater than or equal to 1:40 or a pre-vaccination titre greater than or equal to 1:10 and at least a 4-fold increase in post-vaccination titre. Day 0 was used as reference activity.

End point type	Secondary

End point timeframe:

At Day 189

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	68	108
Units: Subjects	58	47	64	84

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of subjects seroconverted for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point description:

A seroconverted subject was defined as a subject who had either a pre-vaccination titer below 1:10 and a post-vaccination titer greater than or equal to 1:40 or a pre-vaccination titer greater than or equal to 1:10 and at least a 4-fold increase in post-vaccination titer. Day 182 was used as reference activity.

End point type	Secondary

End point timeframe:

At Day 189

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	68	108
Units: Subjects	17	18	9	11

Statistical analyses

No statistical analyses for this end point

Secondary: The number of subjects seroprotected for HI antibodies against Flu A/CAL/7/09 H1N1

End point title	The number of subjects seroprotected for HI antibodies against Flu A/CAL/7/09 H1N1

End point description:

A seroprotected subject was defined as a subject with a serum HI titre greater than or equal to 1:40 that usually is accepted as indicating protection.

End point type	Secondary

End point timeframe:

At Day 0 and Day 42

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	65	68	108
Units: Subjects				
Day 0	27	35	30	48
Day 42	65	64	68	105

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected to HI antibodies against Flu A/CAL/7/09 H1N1

End point title	Number of subjects seroprotected to HI antibodies against Flu A/CAL/7/09 H1N1

End point description:

A seroprotected subject was defined as a subject with a serum HI titre greater than or equal to 1:40

that usually is accepted as indicating protection.

End point type	Secondary

End point timeframe:

At Day 0 and Day 182

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	65	68	109
Units: Subjects				
Day 0	26	36	30	49
Day 182	62	61	67	98

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected to HI antibodies against Flu A/CAL/7/09 H1N1

End point title	Number of subjects seroprotected to HI antibodies against Flu A/CAL/7/09 H1N1

End point description:

A seroprotected subject was defined as a subject with a serum HI titer greater than or equal to 1:40 that usually is accepted as indicating protection.

End point type	Secondary

End point timeframe:

At Day 0, Day 182 and Day 189

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	68	108
Units: Subjects				
Day 0	26	34	30	48
Day 182	61	59	67	97
Day 189	63	63	68	105

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean fold rise (GMFR) for HI antibodies against Flu A/CAL/7/09 H1N1

End point title	Geometric mean fold rise (GMFR) for HI antibodies against Flu A/CAL/7/09 H1N1

End point description:

At Day 42

End point type	Secondary

End point timeframe:

GMFR (also known as the seroconversion factor, SCF) 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 values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	65	68	108
Units: Fold increase				
geometric mean (confidence interval 95%)	27.6 (20.7 to 36.7)	14.2 (10.2 to 19.8)	41.8 (29.4 to 59.3)	19.3 (14.7 to 25.5)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR for HI antibodies against Flu A/CAL/7/09 H1N1

End point title	GMFR for HI antibodies against Flu A/CAL/7/09 H1N1

End point description:

GMFR (also known as the seroconversion factor, SCF) 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

End point timeframe:

At Day 182

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	65	68	109
Units: Fold increase				
geometric mean (confidence interval 95%)	10.5 (7.9 to 14)	5.1 (3.7 to 6.9)	13.6 (9.9 to 18.8)	7.8 (5.8 to 10.3)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR for HI antibodies against Flu A/CAL/7/09 H1N1 using Day 0 as reference activity

End point title	GMFR for HI antibodies against Flu A/CAL/7/09 H1N1 using Day 0 as reference activity

End point description:

GMFR (also known as the seroconversion factor, SCF) 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

End point timeframe:

At Day 189

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	68	108
Units: Fold increase				
geometric mean (confidence interval 95%)	25.2 (17.9 to 35.3)	12.4 (8.3 to 18.6)	23.6 (16.6 to 33.6)	12.1 (9.3 to 15.9)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR for HI antibodies against Flu A/CAL/7/09 H1N1 using Day 182 as reference activity

End point title	GMFR for HI antibodies against Flu A/CAL/7/09 H1N1 using Day 182 as reference activity

End point description:

GMFR (also known as the seroconversion factor, SCF) 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

End point timeframe:

At Day 189

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	68	108
Units: Fold increase				
geometric mean (confidence interval 95%)	2.5 (2 to 3.1)	2.4 (1.9 to 3)	1.7 (1.5 to 2)	1.5 (1.3 to 1.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local Adverse events (AEs)

End point title	Number of subjects reporting any and grade 3 solicited local Adverse events (AEs)

End point description:

Any was defined as occurrence of any local symptom regardless of their intensity grade.Grade 3 redness and swelling was > 100 millimeter (mm) and grade 3 pain was defined as pain that prevented normal activity.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	68	110
Units: Subjects				
Any pain	52	48	61	51
Grade 3 pain	2	0	2	0
Any Redness	2	0	1	0
Grade 3 Redness	0	0	0	0
Any Swelling	4	1	6	1
Grade 3 Swelling	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local AEs

End point title	Number of subjects reporting any and grade 3 solicited local AEs

End point description:

Any was defined as occurrence of any local symptom regardless of their intensity grade.Grade 3 redness and swelling was > 100 millimeter (mm) and grade 3 pain was defined as pain that prevented normal activity

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following booster dose

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	65	68	110
Units: Subjects				
Any Pain	48	40	54	49
Grade 3 Pain	3	3	4	0
Any Redness	4	1	1	0
Grade 3 Redness	0	0	0	0
Any Swelling	6	5	3	0
Grade 3 Swelling	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general AEs

End point title	Number of subjects reporting any, grade 3 and related solicited general AEs

End point description:

Solicited general symptoms assessed were arthralgia, fatigue, gastrointestinal, headache, myalgia, shivering, sweating and fever (Fever = axillary temperature equal to or above 38.0 degrees Celsius (°C)). Any = any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related = symptoms considered by the investigator to have a causal relationship to vaccination. Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 fever = axillary temperature equal to or above (≥) 39.0°C.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	68	110
Units: Subjects				
Any Arthralgia	5	7	6	13
Grade 3 Arthralgia	0	0	0	0
Related Arthralgia	5	6	5	10
Any Fatigue	26	19	24	36
Grade 3 Fatigue	0	0	1	1
Related Fatigue	23	16	21	28
Any Gastrointestinal	5	3	9	8
Grade 3 Gastrointestinal	0	0	1	0
Related Gastrointestinal	3	2	6	5
Any Headache	27	21	39	45
Grade 3 Headache	0	1	0	0
Related Headache	23	16	27	31
Any Myalgia	17	20	28	21

Grade 3 Myalgia	0	0	0	0
Related Myalgia	16	17	23	16
Any Shivering	6	5	8	16
Grade 3 Shivering	0	0	0	0
Related Shivering	6	4	7	11
Any Sweating	6	8	11	15
Grade 3 Sweating	0	0	0	0
Related Sweating	6	3	8	8
Any Fever	2	0	1	3
Grade 3 Fever	0	0	0	1
Related Fever	2	0	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general AEs

End point title	Number of subjects reporting any, grade 3 and related solicited general AEs

End point description:

Solicited general symptoms assessed were arthralgia, fatigue, gastrointestinal, headache, myalgia, shivering, sweating and fever (Fever = axillary temperature equal to or above 38.0 degrees Celsius (°C)). Any = any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related = symptoms considered by the investigator to have a causal relationship to vaccination. Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 fever = axillary temperature equal to or above (≥) 39.0°C.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following booster dose

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65[4]	65[5]	68	110
Units: Subjects				
Any Arthralgia	13	8	12	8
Grade 3 Arthralgia	0	0	0	0
Related Arthralgia	13	5	8	6
Any Fatigue	29	20	28	19
Grade 3 Fatigue	1	0	0	0
Related Fatigue	27	15	25	16
Any Gastrointestinal	4	2	8	5
GRade 3 Gastrointestinal	1	0	0	0
Related Gastrointestinal	4	2	7	3
Any Headache	24	23	32	25
Grade 3 Headache	1	1	0	0
Related Headache	23	16	24	18
Any Myalgia	19	16	17	20

Grade 3 Myalgia	0	0	0	0
Related Myalgia	19	14	15	16
Any Shivering	9	13	15	9
Grade 3 Shivering	0	0	0	0
Related Shivering	9	8	12	8
Any Sweating	5	3	4	9
Grade 3 Sweating	0	0	0	0
Related Sweating	5	3	3	6
Any Fever	11	5	7	2
Grade 3 Fever	0	1	0	0
Related Fever	10	1	6	2

Notes:

[4] - 1 subject moved out of the study area thereby withdrawing from the study.

[5] - 1 subject moved out of the study area thereby withdrawing from the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any Medically Attended Events (MAEs

End point title	Number of subjects reporting any Medically Attended Events (MAEs

End point description:

MAEs were defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason.

End point type	Secondary

End point timeframe:

During the entire study period (Days 0-364) following the first vaccination

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	68	110
Units: Subjects				
Any MAEs	20	21	22	34

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting Potential Immune-Mediated Diseases (pIMDs)

End point title	Number of subjects reporting Potential Immune-Mediated Diseases (pIMDs)

End point description:

pIMDs were defined as a subset of AEs that included both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology.

End point type	Secondary

End point timeframe:

During the entire study period (Days 0-364) following first vaccination

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	68	110
Units: Subjects				
Any pIMDs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal hematological and biochemical parameters assessed with respect to normal laboratory ranges

End point title	Number of subjects with normal and abnormal hematological and biochemical parameters assessed with respect to normal laboratory ranges

End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 21, Day 42, Day 182 and Day 189 which were within normal, above normal, below the normal ranges or unknown.
The laboratory parameters assessed were Alanine aminotransferase (ALAT), Aspartate aminotransferase (ASAT), Total Bilirubin, Creatinine, Hematocrit, Hemoglobin, Platelets, Blood urea nitrogen (BUN) and White blood cells (WBCs).

End point type	Secondary

End point timeframe:

At Days 0, 21, 42, 182 and 189

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66[6]	66[7]	68	110
Units: Subjects				
ALAT, Day 0 Unknown	0	0	0	0
ALAT, Day 0 Below	0	0	0	0
ALAT, Day 0 Within	65	65	66	108
ALAT, Day 0 Above	1	1	2	2
ALAT, Day 21 Unknown	0	0	0	0
ALAT, Day 21 Below	0	0	0	0
ALAT, Day 21 Within	64	64	64	108
ALAT, Day 21 Above	2	2	4	2
ALAT, Day 42 Unknown	0	0	0	0
ALAT, Day 42 Below	0	0	0	0
ALAT, Day 42 Within	64	66	66	104
ALAT, Day 42 Above	2	0	2	6

ALAT, Day 182 Unknown	0	0	0	0
ALAT, Day 182 Below	0	0	0	0
ALAT, Day 182 Within	64	62	67	109
ALAT, Day 182 Above	1	3	1	1
ALAT, Day 189 Unknown	0	0	0	0
ALAT, Day 189 Below	0	0	0	0
ALAT, Day 189 Within	64	61	67	110
ALAT, Day 189 Above	1	4	1	0
ASAT, Day 0 Unknown	0	0	0	0
ASAT, Day 0 Below	0	0	0	0
ASAT, Day 0 Within	63	62	64	108
ASAT, Day 0 Above	3	4	4	2
ASAT, Day 21 Unknown	0	0	0	0
ASAT, Day 21 Below	0	0	0	0
ASAT, Day 21 Within	61	61	63	104
ASAT, Day 21 Above	5	5	5	6
ASAT, Day 42 Unknown	0	0	0	0
ASAT, Day 42 Below	0	0	0	0
ASAT, Day 42 Within	65	60	67	103
ASAT, Day 42 Above	1	6	1	7
ASAT, Day 182 Unknown	0	0	0	0
ASAT, Day 182 Below	0	0	0	0
ASAT, Day 182 Within	63	61	67	110
ASAT, Day 182 Above	2	4	1	0
ASAT, Day 189 Unknown	0	0	0	0
ASAT, Day 189 Below	0	0	0	0
ASAT, Day 189 Within	64	62	67	110
ASAT, Day 189 Above	1	3	1	0
Total Bilirubin, Day 0 Unknown	0	0	0	0
Total Bilirubin, Day 0 Below	0	0	0	0
Total Bilirubin, Day 0 Within	21	22	19	36
Total Bilirubin, Day 0 Above	3	1	5	3
Total Bilirubin, Day 21 Unknown	0	0	0	0
Total Bilirubin, Day 21 Below	0	0	0	0
Total Bilirubin, Day 21 Within	23	21	21	34
Total Bilirubin, Day 21 Above	1	2	3	5
Total Bilirubin, Day 42 Unknown	0	0	0	0
Total Bilirubin, Day 42 Below	0	0	0	0
Total Bilirubin, Day 42 Within	22	21	20	37
Total Bilirubin, Day 42 Above	2	2	4	2
Total Bilirubin, Day 182 Unknown	0	0	0	0
Total Bilirubin, Day 182 Below	0	0	0	0
Total Bilirubin, Day 182 Within	22	21	21	36
Total Bilirubin, Day 182 Above	2	2	3	3
Total Bilirubin, Day 189 Unknown	0	0	0	0
Total Bilirubin, Day 189 Below	0	0	1	0
Total Bilirubin, Day 189 Within	22	22	21	35
Total Bilirubin, Day 189 Above	2	1	2	4
Creatinine, Day 0 Unknown	0	0	0	0
Creatinine, Day 0 Below	4	2	4	5
Creatinine, Day 0 Within	41	47	46	77
Creatinine, Day 0 Above	21	17	18	28

Creatinine, Day 21 Unknown	0	0	0	0
Creatinine, Day 21 Below	4	5	4	8
Creatinine, Day 21 Within	46	48	45	74
Creatinine, Day 21 Above	16	13	19	28
Creatinine, Day 42 Unknown	0	0	0	0
Creatinine, Day 42 Below	4	3	6	7
Creatinine, Day 42 Within	42	48	43	80
Creatinine, Day 42 Above	20	15	19	23
Creatinine, Day 182 Unknown	0	0	0	0
Creatinine, Day 182 Below	6	5	5	5
Creatinine, Day 182 Within	51	52	53	94
Creatinine, Day 182 Above	8	8	10	11
Creatinine, Day 189 Unknown	0	0	0	0
Creatinine, Day 189 Below	4	6	3	6
Creatinine, Day 189 Within	53	54	52	91
Creatinine, Day 189 Above	8	5	13	13
Hematocrit, Day 0 Unknown	0	0	0	0
Hematocrit, Day 0 Below	6	6	9	11
Hematocrit, Day 0 Within	60	59	59	99
Hematocrit, Day 0 Above	0	1	0	0
Hematocrit, Day 21 Unknown	0	0	0	0
Hematocrit, Day 21 Below	6	6	6	13
Hematocrit, Day 21 Within	59	60	61	95
Hematocrit, Day 21 Above	1	0	1	2
Hematocrit, Day 42 Unknown	0	0	0	0
Hematocrit, Day 42 Below	9	6	7	13
Hematocrit, Day 42 Within	57	60	61	96
Hematocrit, Day 42 Above	0	0	0	1
Hematocrit, Day 182 Unknown	0	0	0	0
Hematocrit, Day 182 Below	10	3	6	8
Hematocrit, Day 182 Within	55	61	62	102
Hematocrit, Day 182 Above	0	1	0	0
Hematocrit, Day 189 Unknown	0	0	0	0
Hematocrit, Day 189 Below	8	3	4	8
Hematocrit, Day 189 Within	57	62	64	102
Hematocrit, Day 189 Above	0	0	0	0
Hemoglobin, Day 0 Unknown	0	0	0	0
Hemoglobin, Day 0 Below	10	8	8	17
Hemoglobin, Day 0 Within	56	57	58	92
Hemoglobin, Day 0 Above	0	1	2	1
Hemoglobin, Day 21 Unknown	0	0	0	0
Hemoglobin, Day 21 Below	11	9	7	15
Hemoglobin, Day 21 Within	54	56	59	93
Hemoglobin, Day 21 Above	1	1	2	2
Hemoglobin, Day 42 Unknown	0	0	0	0
Hemoglobin, Day 42 Below	14	8	9	13
Hemoglobin, Day 42 Within	51	57	58	97
Hemoglobin, Day 42 Above	1	1	1	0
Hemoglobin, Day 182 Unknown	0	0	0	0
Hemoglobin, Day 182 Below	10	4	6	12
Hemoglobin, Day 182 Within	54	60	62	98
Hemoglobin, Day 182 Above	1	1	0	0

Hemoglobin, Day 189 Unknown	0	0	0	0
Hemoglobin, Day 189 Below	9	3	4	14
Hemoglobin, Day 189 Within	55	61	64	96
Hemoglobin, Day 189 Above	1	1	0	0
Platelets, Day 0 Unknown	0	0	0	0
Platelets, Day 0 Below	0	0	0	0
Platelets, Day 0 Within	24	23	24	39
Platelets, Day 0 Above	0	0	0	0
Platelets, Day 21 Unknown	0	0	0	0
Platelets, Day 21 Below	1	0	0	1
Platelets, Day 21 Within	23	23	24	37
Platelets, Day 21 Above	0	0	0	1
Platelets, Day 42 Unknown	0	0	0	0
Platelets, Day 42 Below	0	0	0	0
Platelets, Day 42 Within	24	23	24	39
Platelets, Day 42 Above	0	0	0	0
Platelets, Day 182 Unknown	0	0	0	0
Platelets, Day 182 Below	1	0	0	0
Platelets, Day 182 Within	22	23	24	39
Platelets, Day 182 Above	1	0	0	0
Platelets, Day 189 Unknown	0	0	0	0
Platelets, Day 189 Below	0	1	0	0
Platelets, Day 189 Within	23	22	24	39
Platelets, Day 189 Above	1	0	0	0
BUN, Day 0 Unknown	0	0	0	0
BUN, Day 0 Below	3	1	3	0
BUN, Day 0 Within	60	62	63	106
BUN, Day 0 Above	1	0	0	0
BUN, Day 21 Unknown	0	0	0	0
BUN, Day 21 Below	1	1	0	0
BUN, Day 21 Within	63	62	66	106
BUN, Day 21 Above	0	0	0	0
BUN, Day 42 Unknown	0	0	0	0
BUN, Day 42 Below	0	2	1	0
BUN, Day 42 Within	64	60	65	105
BUN, Day 42 Above	0	1	0	1
BUN, Day 182 Unknown	0	0	0	0
BUN, Day 182 Below	0	1	2	0
BUN, Day 182 Within	63	61	64	106
BUN, Day 182 Above	0	0	0	0
BUN, Day 189 Unknown	0	0	0	0
BUN, Day 189 Below	1	3	2	2
BUN, Day 189 Within	62	59	64	104
BUN, Day 189 Above	0	0	0	0
WBCs, Day 0 Unknown	0	0	0	0
WBCs, Day 0 Below	0	3	0	1
WBCs, Day 0 Within	64	54	62	104
WBCs, Day 0 Above	2	9	6	5
WBCs, Day 21 Unknown	0	0	0	0
WBCs, Day 21 Below	3	0	1	2
WBCs, Day 21 Within	56	60	60	103
WBCs, Day 21 Above	7	6	7	5

WBCs, Day 42 Unknown	0	0	0	0
WBCs, Day 42 Below	1	0	0	2
WBCs, Day 42 Within	63	64	64	103
WBCs, Day 42 Above	2	2	4	5
WBCs, Day 182 Unknown	0	0	0	0
WBCs, Day 182 Below	1	1	2	0
WBCs, Day 182 Within	62	60	64	106
WBCs, Day 182 Above	2	4	2	4
WBCs, Day 189 Unknown	0	0	0	0
WBCs, Day 189 Below	0	2	1	1
WBCs, Day 189 Within	62	60	61	105
WBCs, Day 189 Above	3	3	6	4

Notes:

[6] - 1 subject moved out of the study area thereby withdrawing from the study at Days 182 and 189.

[7] - 1 subject moved out of the study area thereby withdrawing from the study at Days 182 and 189.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited AEs

End point title	Number of subjects reporting any unsolicited AEs

End point description:

Unsolicited AE covers any AE 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 any symptom regardless of intensity or relationship to vaccination.

End point type	Secondary

End point timeframe:

During the 42-day (Days 0-41) follow up period after first vaccination.

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	68	110
Units: Subjects				
Any AEs	13	19	22	39

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited AEs

End point title	Number of subjects reporting any unsolicited AEs

End point description:

Unsolicited AE covers any AE 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 any symptom regardless of intensity or relationship to vaccination.

End point type	Secondary

End point timeframe:

During the 21-day (Days 0-20) follow-up period after booster vaccination.

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65[8]	65[9]	68	110
Units: Subjects				
Any AEs	4	7	3	6

Notes:

[8] - 1 subject moved out of the study area thereby withdrawing from the study.

[9] - 1 subject moved out of the study area thereby withdrawing from the study.

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)

End point description:

SAEs: medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the entire study period (Day 0 to Day 364)

End point values	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group	Flu2-2D Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	68	110
Units: Number				
Any SAE(s)	2	2	1	5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs were assessed throughout the study period (Days 0-364). Systematically frequent AEs were assessed 7 days after each vaccination and non-systematically frequent AEs were assessed 42 days after first vaccination and 21 days after booster vaccination.

Adverse event reporting additional description:

1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Flu1-F1-2D Group

Reporting group description:

Subjects received 2 doses of Arepanrix ™ formulation 1 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.

Reporting group title	Flu1-F2-2D Group

Reporting group description:

Subjects received 2 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.

Reporting group title	Flu1-F2-3D Group

Reporting group description:

Subjects received 3 doses of Arepanrix ™ formulation 2 adjuvanted vaccine on Day 0, Day 21 and Day 182 (booster).

Reporting group title	Flu2-2D Group

Reporting group description:

Subjects received 2 doses of Arepanrix ™ unadjuvanted vaccine on Day 0 and Day 182 (booster) and one dose of saline placebo on Day 21.

Serious adverse events	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 66 (3.03%)	2 / 66 (3.03%)	1 / 68 (1.47%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Alcohol poisoning			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 66 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 66 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 66 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal discomfort			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 66 (0.00%)	0 / 66 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 66 (1.52%)	0 / 66 (0.00%)	0 / 68 (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
Renal and urinary disorders			
Facial bones fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 66 (0.00%)	1 / 66 (1.52%)	0 / 68 (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			
Cystitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 66 (1.52%)	0 / 66 (0.00%)	0 / 68 (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
Bronchitis			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 66 (0.00%)	1 / 66 (1.52%)	0 / 68 (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
Appendicitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 66 (0.00%)	0 / 66 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Flu2-2D Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 110 (4.55%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Alcohol poisoning			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal discomfort			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide attempt			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 110 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Facial bones fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 110 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cystitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 110 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 110 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Flu1-F1-2D Group	Flu1-F2-2D Group	Flu1-F2-3D Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 66 (78.79%)	48 / 66 (72.73%)	61 / 68 (89.71%)
General disorders and administration site conditions			
Pain (Primary phase)	Additional description: AE reported during the primary phase of the study		
subjects affected / exposed	52 / 66 (78.79%)	48 / 66 (72.73%)	61 / 68 (89.71%)
occurrences (all)	52	48	61
Swelling (Primary phase)	Additional description: AE reported during the Primary phase of the study		
subjects affected / exposed	6 / 66 (9.09%)	5 / 66 (7.58%)	6 / 68 (8.82%)
occurrences (all)	6	5	6
Redness	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.		
subjects affected / exposed[1]	4 / 65 (6.15%)	1 / 65 (1.54%)	1 / 68 (1.47%)
occurrences (all)	4	1	1
Arthralgia (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[2]	13 / 65 (20.00%)	8 / 65 (12.31%)	12 / 68 (17.65%)
occurrences (all)	13	8	12
Fatigue (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[3]	29 / 65 (44.62%)	20 / 65 (30.77%)	28 / 68 (41.18%)
occurrences (all)	29	20	28
Headache (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	27 / 66 (40.91%)	21 / 66 (31.82%)	39 / 68 (57.35%)
occurrences (all)	27	21	39
Myalgia (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[4]	19 / 65 (29.23%)	16 / 65 (24.62%)	17 / 68 (25.00%)
occurrences (all)	19	16	17
Shivering (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	6 / 66 (9.09%)	5 / 66 (7.58%)	8 / 68 (11.76%)
occurrences (all)	6	5	8
Sweating (Primary phase)	Additional description: AE was reported during the Primary phase of the study.		
subjects affected / exposed	6 / 66 (9.09%)	8 / 66 (12.12%)	11 / 68 (16.18%)
occurrences (all)	6	8	11

Pain (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study		
subjects affected / exposed[5]	48 / 65 (73.85%)	40 / 65 (61.54%)	54 / 68 (79.41%)
occurrences (all)	48	40	54
Swelling (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[6]	6 / 65 (9.23%)	5 / 65 (7.69%)	3 / 68 (4.41%)
occurrences (all)	6	5	3
Arthralgia (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	5 / 66 (7.58%)	7 / 66 (10.61%)	6 / 68 (8.82%)
occurrences (all)	5	7	6
Fatigue (Primary phase)	Additional description: AE was reported during the Primary phase of the study.		
subjects affected / exposed	26 / 66 (39.39%)	19 / 66 (28.79%)	24 / 68 (35.29%)
occurrences (all)	26	19	24
Headache (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[7]	24 / 65 (36.92%)	23 / 65 (35.38%)	32 / 68 (47.06%)
occurrences (all)	24	23	32
Myalgia (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	17 / 66 (25.76%)	20 / 66 (30.30%)	28 / 68 (41.18%)
occurrences (all)	17	20	28
Shivering (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[8]	9 / 65 (13.85%)	13 / 65 (20.00%)	15 / 68 (22.06%)
occurrences (all)	9	13	15
Sweating (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE was reported during the Booster phase of the study.		
subjects affected / exposed[9]	5 / 65 (7.69%)	3 / 65 (4.62%)	4 / 68 (5.88%)
occurrences (all)	5	3	4
Gastrointestinal disorders			
Gastrointestinal (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	5 / 66 (7.58%)	3 / 66 (4.55%)	9 / 68 (13.24%)
occurrences (all)	5	3	9
Gastrointestinal (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group,		

	respectively. AE was reported during the Booster phase of the study.		
subjects affected / exposed[10]	4 / 65 (6.15%)	2 / 65 (3.08%)	8 / 68 (11.76%)
occurrences (all)	4	2	8
Infections and infestations			
Fever	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.		
subjects affected / exposed[11]	11 / 65 (16.92%)	5 / 65 (7.69%)	7 / 68 (10.29%)
occurrences (all)	11	5	7

Non-serious adverse events	Flu2-2D Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 110 (46.36%)		
General disorders and administration site conditions			
Pain (Primary phase)	Additional description: AE reported during the primary phase of the study		
subjects affected / exposed	51 / 110 (46.36%)		
occurrences (all)	51		
Swelling (Primary phase)	Additional description: AE reported during the Primary phase of the study		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences (all)	1		
Redness	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.		
subjects affected / exposed[1]	0 / 110 (0.00%)		
occurrences (all)	0		
Arthralgia (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[2]	8 / 110 (7.27%)		
occurrences (all)	8		
Fatigue (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[3]	36 / 110 (32.73%)		
occurrences (all)	36		
Headache (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	45 / 110 (40.91%)		
occurrences (all)	45		
Myalgia (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.		

	AE reported during the Booster phase of the study.		
subjects affected / exposed[4]	20 / 110 (18.18%)		
occurrences (all)	20		
Shivering (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	16 / 110 (14.55%)		
occurrences (all)	16		
Sweating (Primary phase)	Additional description: AE was reported during the Primary phase of the study.		
subjects affected / exposed	15 / 110 (13.64%)		
occurrences (all)	15		
Pain (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study		
subjects affected / exposed[5]	49 / 110 (44.55%)		
occurrences (all)	49		
Swelling (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[6]	0 / 110 (0.00%)		
occurrences (all)	0		
Arthralgia (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	13 / 110 (11.82%)		
occurrences (all)	13		
Fatigue (Primary phase)	Additional description: AE was reported during the Primary phase of the study.		
subjects affected / exposed	36 / 110 (32.73%)		
occurrences (all)	36		
Headache (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[7]	25 / 110 (22.73%)		
occurrences (all)	25		
Myalgia (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	21 / 110 (19.09%)		
occurrences (all)	21		
Shivering (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE reported during the Booster phase of the study.		
subjects affected / exposed[8]	9 / 110 (8.18%)		
occurrences (all)	9		

Sweating (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE was reported during the Booster phase of the study.		
subjects affected / exposed[9]	9 / 110 (8.18%)		
occurrences (all)	9		
Gastrointestinal disorders			
Gastrointestinal (Primary phase)	Additional description: AE reported during the Primary phase of the study.		
subjects affected / exposed	8 / 110 (7.27%)		
occurrences (all)	8		
Gastrointestinal (Booster phase)	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively. AE was reported during the Booster phase of the study.		
subjects affected / exposed[10]	5 / 110 (4.55%)		
occurrences (all)	5		
Infections and infestations			
Fever	Additional description: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.		
subjects affected / exposed[11]	2 / 110 (1.82%)		
occurrences (all)	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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[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: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: 1 subject moved out of the study area thereby withdrawing from the study in Flu1-F1-2D Group and Flu1-F2-2D Group, respectively.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 November 2009	The protocol was amended for the following reasons: •On the basis of early concordant data from several manufacturers and the United States National Institutes of Health (NIH), it appears that a single 15g dose of unadjuvanted 2009 pandemic H1N1 influenza vaccine is well-tolerated and induces a robust immune response in healthy adults between the ages of three and 64 years. The dose groups were amended in response to these reports and a preliminary finding in children from 6 months to < 36 months of age demonstrating the potency of half-volume vaccine (1.9g HA adjuvanted with AS03B) following a single dose of vaccine: 98% seroconversion rate in children 6 months to < 36 months of age following a single dose of half-volume vaccine. •The age range of eligible subjects was changed to align with European Medicines Agency (EMEA) guideline for pandemic H1N1 vaccine. •Passive surveillance for influenza-like illness (ILI) was added to the study objectives in response to a request from EMEA. Nose and throat swab specimens were collected from subjects with any ILI in order to describe the occurrence of laboratory-confirmed H1N1 cases from the first dose (Day 0) through Day 182 and to genetically sequence viruses causing illness in case of non-study evidence for genetic drift. •Persistence of immune responses were evaluated on Day 182 to assess possible advantages to use of the full adult dose (Group A) or longer term advantages to two primary doses (Group C). Booster vaccination on Day 182 allowed an assessment of the effectiveness of primary vaccination(s) based on the presence or absence of anamnestic immune responses on Day 189. •The design incorporated four groups instead of five groups and the sample size decreased from 300 to 280 subjects. Randomization ratio changed from 1:1:1:1:2 to 3:3:3:5.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported