Clinical trial results:
A Multi-center, Randomized, Single-blind, Dose-Ranging Study to Evaluate Immunogenicity, Safety and Tolerability of Different Doses of Adjuvanted Cell-Derived, Inactivated Novel Swine Origin A/H1N1 Monovalent Subunit Influenza Virus Vaccine in Healthy Japanese Pediatric Subjects.

Summary

EudraCT number	2014-005075-88
Trial protocol	Outside EU/EEA
Global end of trial date	10 December 2009

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	03 May 2015
Version creation reason	• Correction of full data set Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required. Moreover, a change in system user for this study is necessary.

Trial information

Trial identification

Sponsor protocol code	V110_08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01000207
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma K.K
Sponsor organisation address	Minato-ku, Tokyo, Japan, 106-8618
Public contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l, RegistryContactVaccinesUS@novartis.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	22 March 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 December 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To identify the preferred vaccine dose (of antigen and adjuvant) and schedule (one or two administrations) of the cell-derived H1N1sw monovalent vaccine (FCC101) in healthy children/adolescents based on EMEA/CHMP criteria, and safety & tolerability.

Protection of trial subjects:

This trial was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines, the applicable regulatory requirements (s) for the country in which the study is conducted, and applicable standard operating procedures (SOPs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 123
Worldwide total number of subjects	123
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)	14
Children (2-11 years)	76
Adolescents (12-17 years)	30
Adults (18-64 years)	3

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 5 sites in Japan.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	3.75_halfMF59

Arm description:

Subjects received two doses of cell-derived H1N1sw vaccine containing 3.75µg + half MF59.

Arm type	Experimental
Investigational medicinal product name	H1N1 Vaccine
Investigational medicinal product code	V110
Other name	FCC 101
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.25mL doses of H1N1 vaccine (3.75mcg of H1N1 and half MF59) administered three weeks apart. All vaccinations were administered IM in the deltoid muscle or alternative area, preferably of the non-dominant arm at the first vaccination and of the opposite arm to the first vaccination, as a rule, at the second vaccination. For children less than 12 months of age, investigator administered the vaccine into the anterolateral aspect of the thigh (or alternative area).

Arm title	7.5_fullMF59

Arm description:

Subjects received two doses of cell-derived H1N1sw vaccine containing 7.5µg + full MF59.

Arm type	Experimental
Investigational medicinal product name	H1N1 Vaccine
Investigational medicinal product code	V110
Other name	FCC 101
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of two 0.5mL doses of H1N1 vaccine (7.5mcg of H1N1 and full MF59) administered three weeks apart. All vaccinations were administered IM in the deltoid muscle or alternative area, preferably of the non-dominant arm at the first vaccination and of the opposite arm to the first vaccination, as a rule, at the second vaccination. For children less than 12 months of age, investigator administered the vaccine into the anterolateral aspect of the thigh (or alternative area).

Number of subjects in period 1	3.75_halfMF59	7.5_fullMF59
Started	61	62
Completed	59	59
Not completed	2	3
Consent withdrawn by subject	1	-
unable to clasify	1	-
Adverse event, non-fatal	-	2
uable to clasify	-	1

Baseline characteristics

Reporting groups	
Reporting group title	3.75_halfMF59
Reporting group description:	
Subjects received two doses of cell-derived H1N1sw vaccine containing 3.75µg + half MF59.	
Reporting group title	7.5_fullMF59
Reporting group description:	
Subjects received two doses of cell-derived H1N1sw vaccine containing 7.5µg + full MF59.	

Reporting group values	3.75_halfMF59	7.5_fullMF59	Total
Number of subjects	61	62	123
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: years			
arithmetic mean	8	8.6	
standard deviation	± 4.6	± 5.4	-
Gender categorical Units: Subjects			
Female	32	28	60
Male	29	34	63

End points

End points reporting groups

Reporting group title	3.75_halfMF59

Reporting group description:

Subjects received two doses of cell-derived H1N1sw vaccine containing 3.75µg + half MF59.

Reporting group title	7.5_fullMF59

Reporting group description:

Subjects received two doses of cell-derived H1N1sw vaccine containing 7.5µg + full MF59.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the All Randomized Set who actually received a study vaccination, and provided at least one evaluable serum sample both before and after baseline. In case of vaccination not done according to randomization, subjects were analyzed as randomized in the FAS.

Subject analysis set title	Per protocol population- Immunogenicity
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the FAS who receive all the relevant doses of vaccine correctly, and provide evaluable serum samples at the relevant time points, and have no major protocol violation as pre-specified in the Analysis Plan.
A major deviation is defined as a protocol deviation that is considered to have a significant impact on the immunogenicity result of the subject.
The PPS was defined for the entire study and not limited to one visit.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who actually received a study vaccination who provided post-baseline safety data.

Primary: Percentage of subjects achieving seroconversion or a significant increase on day 22 and day 43 as measured by Hemagglutination Inhibition assay (HI).

End point title	Percentage of subjects achieving seroconversion or a significant increase on day 22 and day 43 as measured by Hemagglutination Inhibition assay (HI).[1]

End point description:

Percentage of subjects achieving seroconversion or a significant increase (defined as: HI ≥1:40 for subjects negative at baseline [<1:10]; a minimum 4-fold increase in HI titre for subjects positive at baseline [HI≥1:10]) on day 22 and day 43.
Seroconversion is defined as negative pre-vaccination serum (<10 for HI) / positive postvaccination titer (≥40 for HI). Significant increase in antibody titer/area is defined as at least a fourfold increase in HI from non-negative pre-vaccination serum (≥10 for HI).

End point type	Primary

End point timeframe:

Measured at day 22 and day 43.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	3.75_halfMF59	7.5_fullMF59		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	59		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 22	56.1 (42.4 to 69.3)	76.4 (63 to 86.8)		
Day 43	100 (93.7 to 100)	100 (93.5 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects achieving seroprotection (i.e., HI titer ≥1:40).

End point title	Percentage of subjects achieving seroprotection (i.e., HI titer ≥1:40).[2]

End point description:

Percentage of subjects achieving seroprotection (i.e., HI titer ≥1:40) on Day 1, Day 22 and Day 43.

End point type	Primary

End point timeframe:

At Day 1, Day 22 and Day 43.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	3.75_halfMF59	7.5_fullMF59		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	59		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Day 1	0 (0 to 6.3)	6.8 (1.9 to 16.5)		
Day 22	56.1 (42.4 to 69.3)	78 (65.3 to 87.7)		
Day 43	100 (93.7 to 100)	100 (93.9 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: To evaluate the geometric mean titers on day 1, day 22 and day 43 as measured by HI assay and Microneutralisation (MN) assay.

End point title	To evaluate the geometric mean titers on day 1, day 22 and day 43 as measured by HI assay and Microneutralisation (MN) assay.[3]

End point description:

The immunogenicity was assessed in terms of Geometric Mean Titer (GMT) on Day 1, Day 22 and Day 43 was evaluated by HI and MN assay.

End point type	Primary

End point timeframe:

At Day 1, Day 22 and Day 43

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	3.75_halfMF59	7.5_fullMF59		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	59		
Units: Titers				
geometric mean (confidence interval 95%)				
GMTs (HI) on day 1 (N=57,59)	5.24 (4.58 to 5.99)	6.23 (5.47 to 7.09)		
GMTs (HI) on day 22 (N=57,59)	34 (21 to 54)	84 (53 to 131)		
GMTs (HI) on day 43 (N=57,59)	355 (278 to 453)	596 (471 to 754)		
GMTs (MN) day 1 (N=57,59)	5.2 (4.64 to 5.84)	6.03 (5.4 to 6.74)		
GMTs (MN) day 22 (N=55,58)	31 (20 to 47)	57 (38 to 84)		
GMTs (MN) day 43 (N=57, 58)	288 (226 to 368)	445 (351 to 564)		

Statistical analyses

No statistical analyses for this end point

Primary: To evaluate the geometric mean ratios as measured by HI assay and MN assay.

End point title	To evaluate the geometric mean ratios as measured by HI assay and MN assay.[4]

End point description:

The antibody responses were evaluated in terms of Geometric Mean Ratios (GMR) of post vaccination GMTs versus pre vaccination GMTs by HI and MN assay.

End point type	Primary

End point timeframe:

At day 1, day 22 and day 43.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	3.75_halfMF59	7.5_fullMF59		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	59		
Units: Ratio				
number (confidence interval 95%)				
GMR (HI) - Day 22 to day 1 (N=57,59)	6.45 (4.14 to 10)	13 (8.75 to 21)		
GMR (HI) - Day 43 to day 1 (N=57,59)	68 (52 to 88)	96 (75 to 123)		
GMR (MN) - Day 22 to day 1 (N=55,58)	6.04 (4.08 to 8.93)	9.85 (6.75 to 14)		
GMR (MN) - day 43 to day 1 (N=57,58)	55 (43 to 71)	74 (58 to 94)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with a MN titer ≥1:40, 1:80, and 1:160 and achieving at least 4-fold increase in MN titer.

End point title	Percentage of subjects with a MN titer ≥1:40, 1:80, and 1:160 and achieving at least 4-fold increase in MN titer.[5]

End point description:

Immunogenicity was assessed in terms of percentage of subjects with a MN titer ≥1:40, 1:80, and 1:160 on day 1 and day 43 and percentage of subjects achieving at least a 4-fold increase in MN titer on day 22 and day 43.

End point type	Primary

End point timeframe:

At day 1, day 22 and day 43.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	3.75_halfMF59	7.5_fullMF59		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	59		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Day 1 (≥1:40) (N=57,59)	0 (0 to 6.3)	6.8 (1.9 to 16.5)		
Day 22 (≥1:40) (N=55,58)	45.5 (32 to 59.4)	58.6 (44.9 to 71.4)		
Day 43 (≥1:40) (N=57,58)	98.2 (90.6 to 100)	100 (93.8 to 100)		
Day 1 (≥1:80) (N=57,59)	0 (0 to 6.3)	0 (0 to 6.1)		
Day 22 (≥1:80) (N=55,58)	27.3 (16.1 to 41)	43.1 (30.2 to 56.8)		
Day 43 (≥1:80) (N=57,58)	91.2 (80.7 to 97.1)	98.3 (90.8 to 100)		
Day 1 (≥1:160) (N57,59)	0 (0 to 6.3)	0 (0 to 6.1)		
Day 22 (≥1:160) (N=55,58)	16.4 (7.8 to 28.8)	22.4 (12.5 to 35.3)		
Day 43 (≥1:160) (N=57,58)	70.2 (56.6 to 81.6)	82.8 (70.6 to 91.4)		

Day 22 to day 1 (4-fold increase) (N=55,58)	60 (45.9 to 73)	74.1 (61 to 84.7)		
Day 43 to day 1 (4-fold increase) (N=57,58)	100 (93.7 to 100)	100 (93.8 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting solicited local and systemic reactions after first and second vaccination of subjects aged 6 to 35 months

End point title	Number of subjects reporting solicited local and systemic reactions after first and second vaccination of subjects aged 6 to 35 months[6]

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic reactions 1 week after first and second vaccination of subjects aged 6 to 35 months.

End point type	Primary

End point timeframe:

From day 1 through day 7 after first and second vaccination.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	3.75_halfMF59	7.5_fullMF59		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: number of Subjects				
Any Local (vacc 1)	4	4		
Ecchymosis Any (vacc 1)	2	1		
Ecchymosis 1-10mm (vacc 1)	1	1		
Ecchymosis 11-25mm (vacc 1)	1	0		
Ecchymosis 26-50mm (vacc 1)	0	0		
Ecchymosis 51-100mm (vacc 1)	0	0		
Ecchymosis >100mm (vacc 1)	0	0		
Erythema Any (Vacc 1)	3	3		
Erythema 1-10mm (Vacc 1)	1	1		
Erythema 11-25mm (Vacc 1)	2	1		
Erythema 26-50mm (Vacc 1)	0	0		
Erythema 51-100mm (Vacc 1)	0	1		
Erythema >100 (Vacc 1)	0	0		
Induration Any (Vacc 1)	2	0		
Induration 1-10mm (Vacc 1)	1	0		
Induration 11-25mm (Vacc 1)	1	0		
Induration 26-50mm (Vacc 1)	0	0		
Induration 51-100mm (Vacc 1)	0	0		
Induration >100 (Vacc 1)	0	0		
Swelling Any (Vacc 1)	1	0		
Swelling 1-10mm (Vacc 1)	0	0		
Swelling 11-25mm (vacc 1)	1	0		

Swelling 26-50mm (Vacc 1)	0	0		
Swelling 51-100mm (Vacc 1)	0	0		
Swelling >100mm (Vacc 1)	0	0		
Tenderness (vacc 1)	0	2		
Cried when Injected limb was moved (Vacc 1)	0	0		
Systemic (Vacc 1)	3	4		
Sleepiness (Vacc 1)	3	1		
Diarrhea (Vacc 1)	0	1		
Vomiting (Vacc 1)	1	1		
Irritability (Vacc 1)	1	0		
Change in eating habits (Vacc 1)	2	0		
Shivering (Vacc 1)	0	0		
Unusual Crying (Vacc 1)	1	0		
Other (Vacc 1)	2	0		
Fever Temp (Axillary) (vacc 1)	1	2		
Temp 37.5-37.9 C (Vacc 1)	2	0		
Temp 38.0-38.9 C (Vacc 1)	0	2		
Temp 39.0-39.9 C (Vacc 1)	1	0		
Temp ≥ 40.0 C (Vacc 1)	0	0		
Any Local (vacc 2)	3	3		
Ecchymosis Any (Vacc 2)	1	0		
Ecchymosis 1-10mm (Vacc 2)	1	0		
Ecchymosis 11-25mm (Vacc 2)	0	0		
Ecchymosis 26-50mm (Vacc 2)	0	0		
Ecchymosis 51-100mm (Vacc 2)	0	0		
Ecchymosis >100mm(Vacc 2)	0	0		
Erythema Any (Vacc 2)	3	3		
Erythema 1-10mm (Vacc 2)	0	1		
Erythema 11-25mm (Vacc 2)	1	0		
Erythema 26-50mm (Vacc 2)	1	0		
Erythema 51-100mm (Vacc 2)	1	1		
Erythema >100mm (Vacc 2)	0	1		
Induration Any (Vacc 2)	1	1		
Induration 1-10mm (Vacc 2)	0	0		
Induration 11-25mm (Vacc 2)	0	0		
Induration 26-50mm (Vacc 2)	0	0		
Induration 51-100mm (Vacc 2)	1	1		
Induration >100mm (Vacc 2)	0	0		
Swelling Any (Vacc 2)	2	2		
Swelling 1-10mm (vacc 2)	0	0		
Swelling 11-25mm (Vacc 2)	1	0		
Swelling 26-50mm (Vacc 2)	0	0		
Swelling 51-100mm (Vacc 2)	1	1		
Swelling >100mm (Vacc 2)	0	1		
Tenderness (Vacc 2)	2	2		
Cried when injected limb was moved (Vacc 2)	0	0		
Systemic (Vacc 2)	4	2		
Sleepiness (Vacc 2)	1	0		
Diarrhea (Vacc 2)	1	1		
Vomiting (Vacc 2)	0	0		

Irritability (Vacc 2)	0	0		
Change in eating habits (Vacc 2)	0	0		
Shivering (Vacc 2)	0	0		
Unusual Crying (Vacc 2)	0	0		
Other (Vacc 2)	2	0		
Fever Temp (Axillary) (Vacc 2)	3	2		
Temp 37.5-37.9 C (Vacc 2)	2	2		
Temp 38.0-38.9 C (Vacc 2)	0	2		
Temp 39.0-39.9 C (Vacc 2)	3	0		
Temp ≥ 40.0 C (Vacc 2)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting Solicited local and systemic reactions after first and second vaccination of 3 to 19 years of age

End point title	Number of subjects reporting Solicited local and systemic reactions after first and second vaccination of 3 to 19 years of age[7]

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic reactions 1 week after first and second vaccination of subjects age 3 to 19 years.

End point type	Primary

End point timeframe:

From day 1 through day 7 after first and second vaccination .

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	3.75_halfMF59	7.5_fullMF59		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	51		
Units: Number of subjects				
Any Local (Vacc 1)	39	44		
Ecchymosis Any (Vacc 1)	3	4		
Ecchymosis 1-10mm (Vacc 1)	2	2		
Ecchymosis 11-25mm (Vacc 1)	1	1		
Ecchymosis 26-50mm (Vacc 1)	0	0		
Ecchymosis 51-100mm (Vacc 1)	0	1		
Ecchymosis >100mm (Vacc 1)	0	0		
Erythema Any (Vacc 1)	16	21		
Erythema 1-10mm (Vacc 1)	3	5		
Erythema 11-25mm (Vacc1)	3	1		
Erythema 26-50mm (Vacc 1)	4	9		
Erythema 51-100mm (Vacc 1)	6	6		
Erythema >100mm (Vacc 1)	0	0		
Induration Any (Vacc 1)	9	12		
Induration 1-10mm (Vacc 1)	4	6		

Induration 11-25mm (Vacc 1)	1	3		
Induration 26-50mm (Vacc 1)	2	2		
Induration 51-100mm (Vacc 1)	2	1		
Induration >100mm (Vacc 1)	0	0		
Swelling Any (Vacc 1)	14	18		
Swelling 1-10mm (Vacc 1)	2	5		
Swelling 11-25mm (Vacc 1)	1	1		
Swelling 26-50mm (Vacc 1)	8	9		
Swelling 51-100mm (Vacc 1)	3	3		
Swelling >100mm (Vacc 1)	0	0		
Pain (Vacc 1)	32	42		
Systemic (Vacc 1)	21	22		
Chills (Vacc 1)	2	4		
Malaise (Vacc 1)	7	8		
Myalgia (Vacc 1)	4	9		
Arthralgia (Vacc 1)	1	4		
Headache (Vacc 1)	11	11		
Sweating (Vacc 1)	1	1		
Fatigue (Vacc 1)	8	11		
Nausea (Vacc 1)	1	4		
Other (Vacc 1)	5	5		
Fever Temp (Axilliary) (Vacc 1)	4	5		
Temp 37.5-37.9 C (Vacc 1)	0	3		
Temp 38.0-38.9 C (Vacc 1)	3	2		
Temp 39.0-39.9 C (Vacc 1)	1	3		
Temp ≥ 40.0 C (Vacc 1)	0	0		
Any Local (Vacc 2)	39	37		
Ecchymosis (vacc 2)	2	6		
Ecchymosis 1-10mm (Vacc 2)	1	2		
Ecchymosis 11-25mm (Vacc 2)	0	0		
Ecchymosis 26-50mm (Vacc 2)	0	2		
Eccymosis 51-100mm (Vacc 2)	1	2		
Eccymosis >100mm (Vacc 2)	0	0		
Erythema Any (Vacc 2)	12	12		
Erythema 1-10mm (Vacc 2)	2	0		
Erythema 11-25mm (Vacc 2)	3	0		
Erythema 26-50mm (Vacc 2)	4	6		
Erythema 51-100mm (Vacc 2)	3	6		
Erythema >100mm (Vacc 2)	0	0		
Induration Any (Vacc 2)	7	8		
Induration 1-10mm (Vacc 2)	3	2		
Induration 11-25mm (Vacc 2)	3	1		
Induration 26-50mm (Vacc 2)	0	2		
Induration 51-100mm (Vacc 2)	1	3		
Induration >100mm (Vacc 2)	0	0		
Swelling Any (Vacc 2)	13	16		
Swelling 1-10mm (Vacc 2)	1	0		
Swelling 11-25mm (Vacc 2)	0	1		
Swelling 26-50mm (Vacc 2)	7	9		
Swelling 51-100mm (Vacc 2)	4	6		
Swelling >100mm (Vacc 2)	1	0		
Pain (Vacc 2)	32	30		

Systemic (Vacc 2)	12	16		
Chills (Vacc 2)	1	3		
Malaise (Vacc 2)	5	10		
Myalgia (Vacc 2)	3	6		
Arthalgia (Vacc 2)	0	1		
Headache (Vacc 2)	3	8		
Sweating (Vacc 2)	1	0		
Fatigue (Vacc 2)	5	6		
Nausea (Vacc 2)	3	1		
Other (Vacc 2)	1	5		
Fever Temp (Axillary) (Vacc 2)	1	3		
Temp 37.5-37.9 C (Vacc 2)	0	1		
Temp 38.0-38.9 C (Vacc 2)	1	3		
Temp 39.0-39.9 C (Vacc 2)	0	0		
Temp ≥ 40.0 C (Vacc 2)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to Day 43.	
Adverse event reporting additional description:	
Solicited AEs were collected systematically and the unsolicited AEs were collected non-systemically.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	3.75_halfMF59
Reporting group description:	
Subjects received two doses of cell-derived H1N1sw vaccine containing 3.75µg + half MF59.	
Reporting group title	7.5_fullMF59
Reporting group description:	
Subjects received two doses of cell-derived H1N1sw vaccine containing 7.5µg + full MF59.	

Serious adverse events	3.75_halfMF59	7.5_fullMF59	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 60 (3.33%)	3 / 62 (4.84%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Humerus Fracture	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	0 / 60 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	2 / 60 (3.33%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	3.75_halfMF59	7.5_fullMF59	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 60 (95.00%)	57 / 62 (91.94%)	
Nervous system disorders			
Headache	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	13 / 60 (21.67%)	15 / 62 (24.19%)	
occurrences (all)	19	22	
Somnolence	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	4 / 60 (6.67%)	1 / 62 (1.61%)	
occurrences (all)	5	1	
General disorders and administration site conditions			
Chills	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	3 / 60 (5.00%)	7 / 62 (11.29%)	
occurrences (all)	3	8	
Fatigue	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	9 / 60 (15.00%)	17 / 62 (27.42%)	
occurrences (all)	13	24	
Injection Site Erythema	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	27 / 60 (45.00%)	27 / 62 (43.55%)	
occurrences (all)	35	40	
Injection Site Haemorrhage	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	7 / 60 (11.67%)	10 / 62 (16.13%)	
occurrences (all)	8	12	
Injection Site Induration	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	12 / 60 (20.00%)	18 / 62 (29.03%)	
occurrences (all)	19	21	
Injection Site Pain	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	41 / 60 (68.33%)	46 / 62 (74.19%)	
occurrences (all)	66	79	
Injection Site Pruritus	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	5 / 60 (8.33%)	7 / 62 (11.29%)	
occurrences (all)	6	8	
Injection Site Swelling	Additional description: Occurrences table was generated by using MedDRA version 17.1.		

subjects affected / exposed	22 / 60 (36.67%)	26 / 62 (41.94%)	
occurrences (all)	30	36	
Malaise	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	12 / 60 (20.00%)	16 / 62 (25.81%)	
occurrences (all)	14	18	
Pyrexia	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	11 / 60 (18.33%)	12 / 62 (19.35%)	
occurrences (all)	14	13	
Gastrointestinal disorders			
Nausea	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	4 / 60 (6.67%)	5 / 62 (8.06%)	
occurrences (all)	4	7	
Respiratory, thoracic and mediastinal disorders			
Upper Respiratory Tract Inflammation	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	3 / 60 (5.00%)	6 / 62 (9.68%)	
occurrences (all)	3	7	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	1 / 60 (1.67%)	6 / 62 (9.68%)	
occurrences (all)	1	6	
Myalgia	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	5 / 60 (8.33%)	12 / 62 (19.35%)	
occurrences (all)	7	19	
Infections and infestations			
Bronchitis	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	1 / 60 (1.67%)	6 / 62 (9.68%)	
occurrences (all)	1	6	
Nasopharyngitis	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	3 / 60 (5.00%)	7 / 62 (11.29%)	
occurrences (all)	3	8	
Pharyngitis	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	4 / 60 (6.67%)	1 / 62 (1.61%)	
occurrences (all)	5	1	

Upper Respiratory Tract Infection	Additional description: Occurrences table was generated by using MedDRA version 17.1.		
subjects affected / exposed	4 / 60 (6.67%)	1 / 62 (1.61%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/20586002

http://www.ncbi.nlm.nih.gov/pubmed/22472791