



Clinical trial results:

Estudio fase III, no aleatorizado, abierto para evaluar la seguridad e inmunogenicidad de la vacuna H1N1 adyuvada con AS03A administrada como primovacunación y booster en sujetos entre 3 y 17 años de edad.

Summary

EudraCT number	2009-013785-52
Trial protocol	ES
Global end of trial date	27 November 2010

Results information

Result version number	v2 (current)
This version publication date	17 April 2016
First version publication date	29 May 2015
Version creation reason	• Correction of full data set Data corrected for GMT and general AEs tables and aligned with CTRS data.

Trial information

Trial identification

Sponsor protocol code	113528
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00964158
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 Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000725-PIP01-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 April 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2010
Global end of trial reached?	Yes
Global end of trial date	27 November 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate whether the haemagglutination inhibition (HI) immune response to the vaccine-homologous virus of the Flu Pan vaccine meets or exceeds the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) criteria* 21 days post dose 2 vaccination.

The CHMP criteria are fulfilled if the point estimate for seroconversion rate (SCR) is > 40%, the point estimate for seroprotection rate (SPR) is > 70% and the point estimate for seroconversion factor (SCF) is > 2.5.

Protection of trial subjects:

Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 September 2009
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	Spain: 210
Worldwide total number of subjects	210
EEA total number of subjects	210

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)	210
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Flu Pan 3-5 Years Group

Arm description:

Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 3 to 5 years old.

Arm type	Experimental
Investigational medicinal product name	GSK2340272A vaccine
Investigational medicinal product code	
Other name	Pandemic influenza vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two primary intramuscular (IM) injections and a booster IM injection administered in the deltoid region of the arm.

Arm title	Flu Pan 6-9 Years Group
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Arm description:

Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 6 to 9 years old.

Arm type	Experimental
Investigational medicinal product name	GSK2340272A vaccine
Investigational medicinal product code	
Other name	Pandemic influenza vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two primary intramuscular (IM) injections and a booster IM injection administered in the deltoid region of the arm.

Arm title	Flu Pan 10-17 Years Group
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Arm description:

Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 10 to 17 years old.

Arm type	Experimental
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Investigational medicinal product name	GSK2340272A vaccine
Investigational medicinal product code	
Other name	Pandemic influenza vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two primary intramuscular (IM) injections and a booster IM injection administered in the deltoid region of the arm.

Number of subjects in period 1	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group
Started	53	57	100
Completed	53	56	92
Not completed	0	1	8
Consent withdrawn by subject	-	1	8

Baseline characteristics

Reporting groups

Reporting group title	Flu Pan 3-5 Years Group
Reporting group description:	
Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 3 to 5 years old.	
Reporting group title	Flu Pan 6-9 Years Group
Reporting group description:	
Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 6 to 9 years old.	
Reporting group title	Flu Pan 10-17 Years Group
Reporting group description:	
Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 10 to 17 years old.	

Reporting group values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group
Number of subjects	53	57	100
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	3.5	7.5	13.3
standard deviation	± 0.7	± 1.18	± 2.23
Gender categorical			
Units: Subjects			
Female	31	25	61
Male	22	32	39

Reporting group values	Total		
Number of subjects	210		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	117		
Male	93		

End points

End points reporting groups

Reporting group title	Flu Pan 3-5 Years Group
Reporting group description: Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 3 to 5 years old.	
Reporting group title	Flu Pan 6-9 Years Group
Reporting group description: Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 6 to 9 years old.	
Reporting group title	Flu Pan 10-17 Years Group
Reporting group description: Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule, at 10 to 17 years old.	
Subject analysis set title	Flu Pan Group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule.	

Primary: Haemagglutination inhibition (HI) antibody titers against H1N1 strain

End point title	Haemagglutination inhibition (HI) antibody titers against H1N1 strain ^[1]
End point description:	
End point type	Primary
End point timeframe: At Day 0 and Day 42	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.	

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	198			
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/2009, Day 0 [N=198]	7.4 (6.4 to 8.5)			
Flu A/CAL/7/2009, Day 42 [N=194]	1538.5 (1419 to 1668.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with HI antibody titers $\geq 1:10$

End point title	Number of subjects with HI antibody titers $\geq 1:10$ ^[2]
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End point description:

End point type	Primary
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End point timeframe:

At Day 0 and Day 42

Notes:

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

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

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	198			
Units: Subjects				
Flu A/CAL/7/2009, Day 0 [N=198]	40			
Flu A/CAL/7/2009, Day 42 [N=194]	194			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects in terms of HI antibodies

End point title	Number of seroconverted subjects in terms of HI antibodies ^[3]
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End point description:

The vaccine strain assessed was Flu A/California/7/2009 (H1N1). A seroconverted subject was a subject who had either a pre-vaccination (Day 0) titre less than (<) 1:10 and a post-vaccination titre greater than or equal to (≥) 1:40 or a pre-vaccination titre ≥ 1:10 and at least a 4-fold increase in post-vaccination titre.

End point type	Primary
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End point timeframe:

At Day 42

Notes:

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

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

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	194			
Units: Subjects				
Flu A/CAL/7/2009 [Day 42]	191			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for HI antibodies

End point title	Number of seroprotected subjects for HI antibodies ^[4]
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End point description:

Fluarix vaccine strain was Flu A/California/7/2009 (H1N1). A seroprotected subject was a subject with a serum HI titre $\geq 1:40$ that usually is accepted as indicating protection.

End point type	Primary
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End point timeframe:

At Day 42

Notes:

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

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

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	194			
Units: Subjects				
Flu A/CAL/7/2009 [Day 42]	194			

Statistical analyses

No statistical analyses for this end point

Primary: Seroconversion factor for HI antibody titre

End point title	Seroconversion factor for HI antibody titre ^[5]
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End point description:

The vaccine strain assessed was Flu A/California/7/2009 (H1N1). Seroconversion factor was defined as a serum HI GMTs post-vaccination compared to pre-vaccination. The criterion is fulfilled if the point estimate for SCF was > 2.5 in subjects 18 to 60 years of age.

End point type	Primary
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End point timeframe:

At Day 42

Notes:

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

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

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	194			
Units: Fold increase				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/09 [Day 42]	208.5 (179 to 242.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titers

End point title	HI antibody titers
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End point description:

End point type	Secondary
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End point timeframe:

At Day 0, Day 21, Day 42 and Month 12

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	179			
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/2009 Day 0 [N=179]	7.1 (6.2 to 8.1)			
Flu A/CAL/7/2009 Day 21 [N=178]	347.3 (301.8 to 399.6)			
Flu A/CAL/7/2009 Day 42 [N=173]	1108.1 (1016.6 to 1207.8)			
Flu A/CAL/7/2009 Month 12 [N=179]	167.3 (147.2 to 190.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-HIs antibody concentrations $\geq$ 1:10

End point title	Number of subjects with anti-HIs antibody concentrations $\geq$ 1:10
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End point description:

End point type	Secondary
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End point timeframe:

At Day 0, Day 21, Day 42 and Month 12

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	179			
Units: Subjects				
Flu A/CAL/7/2009 Day 0 [N=179]	28			
Flu A/CAL/7/2009 Day 21 [N=178]	178			

Flu A/CAL/7/2009 Day 42 [N=173]	173			
Flu A/CAL/7/2009 Month 12 [N=179]	179			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for HI antibodies

End point title	Number of seroconverted subjects for HI antibodies
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End point description:

End point type	Secondary
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End point timeframe:

At Day 21, Day 42 and Month 12

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	179			
Units: Subjects				
Flu A/CAL/7/09 Day 21 [N=178]	176			
Flu A/CAL/7/09 Day 42 [N=173]	170			
Flu A/CAL/7/09 Month 12 [N=179]	172			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for HI antibodies

End point title	Number of seroprotected subjects for HI antibodies
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End point description:

End point type	Secondary
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End point timeframe:

At Day 0, Day 21, Day 42 and Month 12

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	179			
Units: Subjects				
Flu A/CAL/7/09 Day 0 [N=179]	15			
Flu A/CAL/7/09 Day 21 [N=178]	178			
Flu A/CAL/7/09 Day 42 [N=173]	173			
Flu A/CAL/7/09 Month 12 [N=179]	178			

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion factor for HI antibody titer

End point title	Seroconversion factor for HI antibody titer
End point description:	
End point type	Secondary
End point timeframe:	
At Day 21, Day 42 and Month 12	

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	179			
Units: Fold increase				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/09 Day 21 [N=178]	49.1 (42.6 to 56.7)			
Flu A/CAL/7/09 Day 42 [N=173]	161.2 (138.5 to 187.6)			
Flu A/CAL/7/09 Month 12 [N=179]	23.7 (20.6 to 27.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum neutralising antibody titres

End point title	Serum neutralising antibody titres
End point description:	
The vaccine strain assessed was A/Netherlands/7/2009(H1N1).	
End point type	Secondary

End point timeframe:

At Day 0, Day 21, Day 42 and Month 12

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	90			
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Neth/602/09 Day 0 [N=90]	5.2 (4.3 to 6.3)			
Flu A/Neth/602/09 Day 21 [N=90]	112.6 (83 to 152.8)			
Flu A/Neth/602/09 Day 42 [N=87]	847.2 (671.1 to 1069.6)			
Flu A/Neth/602/09 Month 12 [N=85]	172 (141.9 to 208.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects in terms of H1N1 neutralizing antibodies

End point title	Number of seroconverted subjects in terms of H1N1 neutralizing antibodies
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End point description:

End point type	Secondary
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End point timeframe:

At Day 21, Day 42 and Month 12

End point values	Flu Pan Group			
Subject group type	Subject analysis set			
Number of subjects analysed	88			
Units: Subjects				
Flu A/Neth/602/09 Day 21 [N=88]	76			
Flu A/Neth/602/09 Day 42 [N=85]	85			
Flu A/Neth/602/09 Month 12 [N=83]	79			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms
End point description:	
End point type	Secondary
End point timeframe:	
During a 7-day follow-up period, i.e., day of vaccination and 6 subsequent days after each vaccination on Day 0 and Day 21	

End point values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	98	
Units: Subjects				
Pain, Dose 1 [N=53,57,98]	40	54	91	
Grade 3 Pain, Dose 1 [N=53,57,98]	2	3	8	
Redness, Dose 1 [N=53,57,98]	15	14	21	
Grade 3 Redness, Dose 1 [N=53,57,98]	0	2	6	
Swelling, Dose 1 [N=53,57,98]	18	16	41	
Grade 3 Swelling, Dose 1 [N=53,57,98]	1	3	6	
Pain, Dose 2 [N=52,57,93]	44	55	90	
Grade 3 Pain, Dose 2 [N=52,57,93]	5	8	12	
Redness, Dose 2 [N=52,57,93]	18	19	26	
Grade 3 Redness, Dose 2 [N=52,57,93]	4	2	2	
Swelling, Dose 2 [N=52,57,93]	16	26	50	
Grade 3 Swelling, Dose 2 [N=52,57,93]	2	1	2	
Pain, Across Doses [N=53,57,98]	47	56	95	
Grade 3 Pain, Across Doses [N=53,57,98]	7	8	16	
Redness, Across Doses [N=53,57,98]	22	22	33	
Grade 3 Redness, Across Doses [N=53,57,98]	4	4	6	
Swelling, Across Doses [N=53,57,98]	25	30	60	
Grade 3 Swelling, Across Doses [N=53,57,98]	3	4	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms ^[6]
End point description:	
End point type	Secondary

End point timeframe:

During a 7-day follow-up period, i.e., day of vaccination and 6 subsequent days after each vaccination on Day 0 and Day 21 in the Flu Pan 3-5 Years Group

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The solicited general symptoms were different for the above 6 years old groups, hence they are presented separately.

End point values	Flu Pan 3-5 Years Group			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Subjects				
Any Diarrhea [N=53] Dose 1	2			
Grade 3 Diarrhea [N=53] Dose 1	0			
Related Diarrhea [N=53] Dose 1	1			
Any Drowsiness [N=53] Dose 1	11			
Grade 3 Drowsiness [N=53] Dose 1	0			
Related Drowsiness [N=53] Dose 1	8			
Any Irritability [N=53] Dose 1	14			
Grade 3 Irritability [N=53] Dose 1	0			
Related Irritability [N=53] Dose 1	10			
Any Loss of appetite [N=53] Dose 1	14			
Grade 3 Loss of appetite [N=53] Dose 1	0			
Related Loss of appetite [N=53] Dose 1	8			
Any Shivering [N=53] Dose 1	5			
Grade 3 Shivering [N=53] Dose 1	0			
Related Shivering [N=53] Dose 1	2			
Any Sweating [N=53] Dose 1	4			
Grade 3 Sweating [N=53] Dose 1	0			
Related Sweating [N=53] Dose 1	1			
Any Temperature [N=53] Dose 1	14			
Grade 3 Temperature [N=53] Dose 1	1			
Related Temperature [N=53] Dose 1	8			
Any Diarrhea [N=52] Dose 2	6			
Grade 3 Diarrhea [N=52] Dose 2	0			
Related Diarrhea [N=52] Dose 2	3			
Any Drowsiness [N=52] Dose 2	17			
Grade 3 Drowsiness [N=52] Dose 2	2			
Related Drowsiness [N=52] Dose 2	15			
Any Irritability [N=52] Dose 2	15			
Grade 3 Irritability [N=52] Dose 2	3			
Related Irritability [N=52] Dose 2	14			
Any Loss of appetite [N=52] Dose 2	21			
Grade 3 Loss of appetite [N=52] Dose 2	3			
Related Loss of appetite [N=52] Dose 2	17			
Any Shivering [N=52] Dose 2	6			
Grade 3 Shivering [N=52] Dose 2	1			
Related Shivering [N=52] Dose 2	5			
Any Sweating [N=52] Dose 2	6			
Grade 3 Sweating [N=52] Dose 2	0			
Related Sweating [N=52] Dose 2	4			

Any Temperature [N=52] Dose 2	26			
Grade 3 Temperature [N=52] Dose 2	2			
Related Temperature [N=52] Dose 2	23			
Any Diarrhea [N=53] Across doses	8			
Grade 3 Diarrhea [N=53] Across doses	0			
Related Diarrhea [N=53] Across doses	4			
Any Drowsiness [N=53] Across doses	22			
Grade 3 Drowsiness [N=53] Across doses	2			
Related Drowsiness [N=53] Across doses	19			
Any Irritability [N=53] Across doses	21			
Grade 3 Irritability [N=53] Across doses	3			
Related Irritability [N=53] Across doses	19			
Any Loss of appetite [N=53] Across doses	28			
Grade 3 Loss of appetite [N=53] Across doses	3			
Related Loss of appetite [N=53] Across doses	21			
Any Shivering [N=53] Across doses	11			
Grade 3 Shivering [N=53] Across doses	1			
Related Shivering [N=53] Across doses	7			
Any Sweating [N=53] Across doses	10			
Grade 3 Sweating [N=53] Across doses	0			
Related Sweating [N=53] Across doses	5			
Any Temperature [N=53] Across doses	33			
Grade 3 Temperature [N=53] Across doses	3			
Related Temperature [N=53] Across doses	26			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms ^[7]
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End point description:

End point type	Secondary
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End point timeframe:

During a 7-day follow-up period, i.e., day of vaccination and 6 subsequent days after each vaccination on Day 0 and Day 21 in the Flu Pan 6-9 Years Group and Flu Pan 10-17 Years Group

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The solicited general symptoms were different for the above 6 years old groups, hence they are presented separately.

End point values	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	98		
Units: Subjects				
Any Arthralgia, Dose 1 [N=57,98]	9	26		
Grade 3 Arthralgia, Dose 1 [N=57,98]	0	1		
Related Arthralgia, Dose 1 [N=57,98]	8	26		
Any Fatigue, Dose 1 [N=57,98]	21	44		
Grade 3 Fatigue, Dose 1 [N=57,98]	1	4		
Related Fatigue, Dose 1 [N=57,98]	20	40		
Any Gastrointestinal, Dose 1 [N=57,98]	13	12		
Grade 3 Gastrointestinal, Dose 1 [N=57,98]	2	1		
Related Gastrointestinal, Dose 1 [N=57,98]	9	6		
Any Headache, Dose 1 [N=57,98]	25	48		
Grade 3 Headache, Dose 1 [N=57,98]	2	3		
Related Headache, Dose 1 [N=57,98]	24	41		
Any Myalgia, Dose 1 [N=57,98]	15	35		
Grade 3 Myalgia, Dose 1 [N=57,98]	2	2		
Related Myalgia, Dose 1 [N=57,98]	13	34		
Any Shivering, Dose 1 [N=57,98]	7	19		
Grade 3 Shivering, Dose 1 [N=57,98]	0	0		
Related Shivering, Dose 1 [N=57,98]	4	14		
Any Sweating, Dose 1 [N=57,98]	2	8		
Grade 3 Sweating, Dose 1 [N=57,98]	0	0		
Related Sweating, Dose 1 [N=57,98]	1	5		
Any Temperature/Axillary, Dose 1 [N=57,98]	13	17		
Grade 3 Temperature/Axillary, Dose 1 [N=57,98]	0	0		
Related Temperature/Axillary, Dose 1 [N=57,98]	10	15		
Any Arthralgia, Dose 2 [N=57,93]	13	34		
Grade 3 Arthralgia, Dose 2 [N=57,93]	1	1		
Related Arthralgia, Dose 2 [N=57,93]	13	32		
Any Fatigue, Dose 2 [N=57,93]	29	50		
Grade 3 Fatigue, Dose 2 [N=57,93]	3	5		
Related Fatigue, Dose 2 [N=57,93]	28	48		
Any Gastrointestinal, Dose 2 [N=57,93]	9	10		
Grade 3 Gastrointestinal, Dose 2 [N- 57,93]	0	0		
Related Gastrointestinal, Dose 2 [N=57,93]	8	6		
Any Headache, Dose 2 [N=57,93]	26	51		
Grade 3 Headache, Dose 2 [N=57,93]	4	5		
Related Headache, Dose 2 [N=57,93]	26	50		
Any Myalgia, Dose 2 [N=57,93]	16	47		
Grade 3 Myalgia, Dose 2 [N=57,93]	1	2		
Related Myalgia, Dose 2 [N=57,93]	16	44		
Any Shivering, Dose 2 [N=57,93]	14	27		
Grade 3 Shivering, Dose 2 [N=57,93]	0	1		
Related Shivering, Dose 2 [N=57,93]	13	25		

Any Sweating, Dose 2 [N=57,93]	7	8		
Grade 3 Sweating, Dose 2 [N=57,93]	0	0		
Related Sweating, Dose 2 [N=57,93]	4	7		
Any Temperature/Axillary, Dose 2 [N=57,93]	20	23		
Grade 3 Temperature/Axillary, Dose 2 [N=57,93]	1	1		
Related Temperature/Axillary, Dose 2 [N=57,93]	19	16		
Any Arthralgia, Across Doses [N=57,98]	20	44		
Grade 3 Arthralgia, Across Doses [N=57,98]	1	2		
Related Arthralgia, Across Doses [N=57,98]	19	43		
Any Fatigue, Across Doses [N=57,98]	35	63		
Grade 3 Fatigue, Across Doses [N=57,98]	4	9		
Related Fatigue, Across Doses [N=57,98]	34	59		
Any Gastrointestinal, Across Doses [N=57,98]	17	16		
Grade 3 Gastrointestinal, Across Doses [N=57,98]	2	1		
Related Gastrointestinal, Across Doses [N=57,98]	14	10		
Any Headache, Across Doses [N=57,98]	34	70		
Grade 3 Headache, Across Doses [N=57,98]	5	6		
Related Headache, Across Doses [N=57,98]	34	64		
Any Myalgia, Across Doses [N=57,98]	23	56		
Grade 3 Myalgia, Across Doses [N=57,98]	2	4		
Related Myalgia, Across Doses [N=57,98]	21	53		
Any Shivering, Across Doses [N=57,98]	19	38		
Grade 3 Shivering, Across Doses [N=57,98]	0	1		
Related Shivering, Across Doses [N=57,98]	15	33		
Any Sweating, Across Doses [N=57,98]	9	14		
Grade 3 Sweating, Across Doses [N=57,98]	0	0		
Related Sweating, Across Doses [N=57,98]	5	11		
Any Temperature/Axillary, Across Doses [N=57,98]	27	33		
Grade 3 Temperature/Axillary, Across Doses [N=57,98]	1	1		
Related Temperature/Axillary, Across Doses [N=57,98]	23	25		

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

During the entire study period

End point values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	100	
Units: Subjects				
MAEs	36	21	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with adverse events of specific interest (AESIs)/potential immune-mediated disease (pIMDs)

End point title	Number of subjects with adverse events of specific interest (AESIs)/potential immune-mediated disease (pIMDs)
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End point description:

End point type	Secondary
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End point timeframe:

During the entire study period

End point values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	100	
Units: Subjects				
AESI(s)/pIMD(s)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal or abnormal values of biochemical parameters

End point title	Number of subjects with normal or abnormal values of biochemical parameters
End point description:	
Biochemical parameters assessed were Alanine Amino Trasferase (ALAT), Aspartate Amino Transferase (ASAT), Bilirubin, Creatinine and Blood Urea Nitrogen (BUN).	
End point type	Secondary
End point timeframe:	
During the entire study period	

End point values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	97	
Units: Subjects				
ALAT, Unknown, Day 0 [N=30,38,59]	0	0	0	
ALAT, Below, Day 0 [N=30,38,59]	0	0	0	
ALAT, Within, Day 0 [N=30,38,59]	30	38	59	
ALAT, Above, Day 0 [N=30,38,59]	0	0	0	
ALAT, Unknown, Day 21 [N=53,57,97]	1	0	2	
ALAT, Below, Day 21 [N=53,57,97]	0	0	0	
ALAT, Within, Day 21 [N=53,57,97]	52	57	94	
ALAT, Above, Day 21 [N=53,57,97]	0	0	1	
ALAT, Unknown, Day 42 [N=52,56,93]	2	1	0	
ALAT, Below, Day 42 [N=52,56,93]	0	0	0	
ALAT, Within, Day 42 [N=52,56,93]	50	55	91	
ALAT, Above, Day 42 [N=52,56,93]	0	0	2	
ASAT, Unknown, Day 0 [N=30,38,59]	0	0	0	
ASAT, Below, Day 0 [N=30,38,59]	0	0	0	
ASAT, Within, Day 0 [N=30,38,59]	28	38	58	
ASAT, Above, Day 0 [N=30,38,59]	2	0	1	
ASAT, Unknown, Day 21 [N=53,57,97]	2	1	2	
ASAT, Below, Day 21 [N=53,57,97]	0	0	0	
ASAT, Within, Day 21 [N=53,57,97]	50	56	94	
ASAT, Above, Day 21 [N=53,57,97]	1	0	1	
ASAT, Unknown, Day 42 [N=52,56,93]	2	1	0	
ASAT, Below, Day 42 [N=52,56,93]	0	0	0	
ASAT, Within, Day 42 [N=52,56,93]	50	55	91	
ASAT, Above, Day 42 [N=52,56,93]	0	0	2	
BILI, Unknown, Day 0 [N=30,38,59]	0	0	0	
BILI, Below, Day 0 [N=30,38,59]	0	0	0	
BILI, Within, Day 0 [N=30,38,59]	30	38	57	
BILI, Above, Day 0 [N=30,38,59]	0	0	2	
BILI, Unknown, Day 21 [N=53,57,97]	1	0	2	
BILI, Below, Day 21 [N=53,57,97]	0	0	0	
BILI, Within, Day 21 [N=53,57,97]	52	57	90	
BILI, Above, Day 21 [N=53,57,97]	0	0	5	
BILI, Unknown, Day 42 [N=52,56,93]	2	1	0	
BILI, Below, Day 42 [N=52,56,93]	0	0	0	
BILI, Within, Day 42 [N=52,56,93]	50	55	90	
BILI, Above, Day 42 [N=52,56,93]	0	0	3	

CREA, Unknown, Day 0 [N=30,38,59]	0	0	0	
CREA, Below, Day 0 [N=30,38,59]	1	0	1	
CREA, Within, Day 0 [N=30,38,59]	28	33	54	
CREA, Above, Day 0 [N=30,38,59]	1	5	4	
CREA, Unknown, Day 21 [N=53,57,97]	1	0	2	
CREA, Below, Day 21 [N=53,57,97]	7	2	1	
CREA, Within, Day 21 [N=53,57,97]	44	53	90	
CREA, Above, Day 21 [N=53,57,97]	1	2	4	
CREA, Unknown, Day 42 [N=52,56,93]	2	1	0	
CREA, Below, Day 42 [N=52,56,93]	5	2	2	
CREA, Within, Day 42 [N=52,56,93]	45	52	85	
CREA, Above, Day 42 [N=52,56,93]	0	1	6	
BUN, Unknown, Day 0 [N=30,38,59]	0	0	0	
BUN, Below, Day 0 [N=30,38,59]	0	0	0	
BUN, Within, Day 0 [N=30,38,59]	28	37	57	
BUN, Above, Day 0 [N=30,38,59]	2	1	2	
BUN, Unknown, Day 21 [N=53,57,97]	1	0	2	
BUN, Below, Day 21 [N=53,57,97]	1	0	0	
BUN, Within, Day 21 [N=53,57,97]	49	52	92	
BUN, Above, Day 21 [N=53,57,97]	2	5	3	
BUN, Unknown, Day 42 [N=52,56,93]	2	1	0	
BUN, Below, Day 42 [N=52,56,93]	0	0	0	
BUN, Within, Day 42 [N=52,56,93]	47	47	89	
BUN, Above, Day 42 [N=52,56,93]	3	8	4	

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

During a 21-day follow-up period after the first vaccination

End point values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	100	
Units: Subjects				
Any AE(s)	29	22	30	
Grade 3 AE(s)	4	2	1	
Related AE(s)	2	4	6	

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

During the 83-day period following first vaccination and the 62-day period following second vaccination

End point values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	100	
Units: Subjects				
Any AE(s)	37	26	41	
Grade 3 AE(s)	8	4	7	
Related AE(s)	2	4	6	

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

During the entire study period

End point values	Flu Pan 3-5 Years Group	Flu Pan 6-9 Years Group	Flu Pan 10-17 Years Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	57	100	
Units: Subjects				
SAEs	0	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.1
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Reporting groups

Reporting group title	Flu Pan 3-5 Years Group
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Reporting group description: -

Reporting group title	Flu Pan 10-17 Years Group
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Reporting group description: -

Reporting group title	Flu Pan 6-9 Years Group
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Reporting group description: -

Serious adverse events	Flu Pan 3-5 Years Group	Flu Pan 10-17 Years Group	Flu Pan 6-9 Years Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)	1 / 100 (1.00%)	0 / 57 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	0 / 53 (0.00%)	1 / 100 (1.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Flu Pan 3-5 Years Group	Flu Pan 10-17 Years Group	Flu Pan 6-9 Years Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 53 (69.81%)	41 / 100 (41.00%)	26 / 57 (45.61%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 53 (5.66%)	5 / 100 (5.00%)	0 / 57 (0.00%)
occurrences (all)	3	5	0
General disorders and administration site conditions			

Pyrexia subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4	0 / 100 (0.00%) 0	1 / 57 (1.75%) 1
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3	0 / 100 (0.00%) 0	1 / 57 (1.75%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 5 0 / 53 (0.00%) 0 0 / 53 (0.00%) 0	4 / 100 (4.00%) 4 0 / 100 (0.00%) 0 0 / 100 (0.00%) 0	3 / 57 (5.26%) 3 3 / 57 (5.26%) 3 3 / 57 (5.26%) 3
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Laryngitis subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Ear infection subjects affected / exposed occurrences (all)	11 / 53 (20.75%) 11 4 / 53 (7.55%) 4 5 / 53 (9.43%) 5 0 / 53 (0.00%) 0 5 / 53 (9.43%) 5 4 / 53 (7.55%) 4	14 / 100 (14.00%) 14 3 / 100 (3.00%) 3 0 / 100 (0.00%) 0 5 / 100 (5.00%) 5 0 / 100 (0.00%) 0 0 / 100 (0.00%) 0	3 / 57 (5.26%) 3 1 / 57 (1.75%) 1 2 / 57 (3.51%) 2 1 / 57 (1.75%) 1 1 / 57 (1.75%) 1 0 / 57 (0.00%) 0

Otitis media			
subjects affected / exposed	3 / 53 (5.66%)	0 / 100 (0.00%)	0 / 57 (0.00%)
occurrences (all)	3	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 April 2010	Amendment 5 Due to recent developments in the pandemic situation and following the feedback from the European authorities, the follow-up study FLU D-PAN H1N1-037 is no longer planned to be conducted. Therefore the protocol was amended to delete all references to this planned follow-up study. In addition an error from the previous amendment has been corrected (Day 21 timepoint removed from primary endpoint in body of protocol).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported