Clinical trial results:
A Phase II, Multicentre, Randomised, Observer-blind Study to Evaluate the Immunogenicity, Safety and Tolerability of CSL's 2009 H1N1 Influenza Vaccine (CSL425) in Healthy Children Aged >= 6 Months to < 9 Years.

Summary

EudraCT number	2014-005183-15
Trial protocol	Outside EU/EEA
Global end of trial date	26 October 2009

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	CSLCT-CAL-09-60

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00940108
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Limited
Sponsor organisation address	45 Poplar Rd, Parkville, Australia, 3052
Public contact	Clinical Program Director, bioCSL, bioCSL LTD PTY, biocsl.clinicaltrials@biocsl.com.au
Scientific contact	Clinical Program Director, bioCSL, bioCSL LTD PTY, biocsl.clinicaltrials@biocsl.com.au

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	16 April 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 October 2009
Global end of trial reached?	Yes
Global end of trial date	26 October 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of the 15 µg haemagglutinin (HA) and 30 µg HA antigen doses of 2009 H1N1 vaccine (H1N1 vaccine) in two cohorts of healthy children: Cohort A: participants aged 6 months to less than 3 years ; Cohort B: participants aged 3 years to less than 9 years.

Protection of trial subjects:

The study protocol, the study protocol amendments, the Participant Information Sheet (PIS) and the Informed Consent Form (ICF) were reviewed and approved by an Independent Ethics Committee (IEC). This study was conducted under an Australian Clinical Trial Notification scheme and documented in accordance with the World Medical Association Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 August 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	Australia: 369
Worldwide total number of subjects	369
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)	101
Children (2-11 years)	268
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:

Active Study Initiation Date: 03 August 2009 (First participant, First Visit)
Active Study Completion Date: 26 October 2009 (Last participant, Visit 3)
The study was conducted at six sites in Australia.

Pre-assignment

Screening details:

One randomized participant withdrew consent prior to vaccine administration and was not included in the participant flow data or in any analysis population.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A (6 months to < 3 years)

Arm description:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1). The vaccine was supplied as a thiomersal-free suspension in pre-filled syringes at a concentration of 60 µg HA antigen per mL.

Arm type	Experimental
Investigational medicinal product name	HIN1 vaccine (15 ug HA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1).
The dose administered was 15 µg HA antigen per 0.25 mL dose.
Participants received two vaccinations of their assigned dose, administered 21 days apart.

Investigational medicinal product name	HIN1 vaccine (30 ug HA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1).
The dose administered was 30 µg HA antigen per 0.5 mL dose.
Participants received two vaccinations of their assigned dose, administered 21 days apart.

Arm title	Cohort B (3 years to < 9 years)

Arm description:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1). The vaccine was supplied as a thiomersal-free suspension in pre-filled syringes at a concentration of 60 µg HA antigen per mL.

Arm type	Experimental

Investigational medicinal product name	HIN1 vaccine (15 ug HA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1).
The dose administered was 15 µg HA antigen per 0.25 mL dose.
Participants received two vaccinations of their assigned dose, administered 21 days apart.

Investigational medicinal product name	HIN1 vaccine (30 ug HA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1).
The dose administered was 30 µg HA antigen per 0.5 mL dose.
Participants received two vaccinations of their assigned dose, administered 21 days apart.

Number of subjects in period 1	Cohort A (6 months to < 3 years)	Cohort B (3 years to < 9 years)
Started	162	207
Completed	148	199
Not completed	14	8
Diagnosed with H1N1	-	1
Consent withdrawn by subject	3	1
Adverse event, non-fatal	6	2
Declined further vaccination	1	3
Refused - pyrexia after Dose 1	1	-
Dose 2 contraindicated	2	1
Viral illness after Dose 1	1	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort A (6 months to < 3 years)

Reporting group description:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1). The vaccine was supplied as a thiomersal-free suspension in pre-filled syringes at a concentration of 60 µg HA antigen per mL.

Reporting group title	Cohort B (3 years to < 9 years)

Reporting group description:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1). The vaccine was supplied as a thiomersal-free suspension in pre-filled syringes at a concentration of 60 µg HA antigen per mL.

Reporting group values	Cohort A (6 months to < 3 years)	Cohort B (3 years to < 9 years)	Total
Number of subjects	162	207	369
Age categorical Units: Subjects			
Cohort A: 6 months to <3 years, 15ug dose	82	0	82
Cohort A: 6 months to <3 years, 30ug dose	80	0	80
Cohort B: 3 years to <9 years, 15 ug dose	0	103	103
Cohort B: 3 years to <9 years, 30 ug dose	0	104	104
Age continuous Units: years			
arithmetic mean	1.71	5.72	
standard deviation	± 0.7	± 1.71	-
Gender categorical Units: Subjects			
Female	82	102	184
Male	80	105	185

Subject analysis sets

Subject analysis set title	CSL425 (15 mcg) Cohort A
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 6 months to less than 3 years received two doses of CSL425 (15 mcg of haemagglutinin antigen per 0.25 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	CSL425 (30 mcg) Cohort A
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 6 months to less than 3 years received two doses of CSL425 (30 mcg of haemagglutinin antigen per 0.5 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	CSL425 (15 mcg) Cohort B
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 3 years to less than 9 years received two doses of CSL425 (15 mcg of haemagglutinin antigen per 0.25 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	CSL425 (30 mcg) Cohort B
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 3 years to less than 9 years received two doses of CSL425 (30 mcg of haemagglutinin antigen per 0.5 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	Total of all reporting groups
Subject analysis set type	Per protocol

Subject analysis set description:

Total of all reporting groups.

Reporting group values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B
Number of subjects	82	80	103
Age categorical			
Units: Subjects			
Cohort A: 6 months to <3 years, 15ug dose	82	0	0
Cohort A: 6 months to <3 years, 30ug dose	0	80	0
Cohort B: 3 years to <9 years, 15 ug dose	0	0	103
Cohort B: 3 years to <9 years, 30 ug dose	0	0	0
Age continuous			
Units: years			
arithmetic mean	1.68	1.73	5.78
standard deviation	± 0.67	± 0.74	± 1.69
Gender categorical			
Units: Subjects			
Female	41	41	53
Male	41	39	50

Reporting group values	CSL425 (30 mcg) Cohort B	Total of all reporting groups	
Number of subjects	104	369	
Age categorical			
Units: Subjects			
Cohort A: 6 months to <3 years, 15ug dose	0	82	
Cohort A: 6 months to <3 years, 30ug dose	0	80	
Cohort B: 3 years to <9 years, 15 ug dose	0	103	
Cohort B: 3 years to <9 years, 30 ug dose	104	104	
Age continuous			
Units: years			
arithmetic mean	5.66	3.96	
standard deviation	± 1.74	± 2.42	

Gender categorical Units: Subjects			
Female	49	184	
Male	55	185	

End points

End points reporting groups

Reporting group title	Cohort A (6 months to < 3 years)

Reporting group description:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1). The vaccine was supplied as a thiomersal-free suspension in pre-filled syringes at a concentration of 60 µg HA antigen per mL.

Reporting group title	Cohort B (3 years to < 9 years)

Reporting group description:

The H1N1 vaccine, a monovalent, inactivated, split-virus vaccine, contains the HA antigen for the influenza strain A/California/7/2009(H1N1)v-like virus (2009 H1N1). The vaccine was supplied as a thiomersal-free suspension in pre-filled syringes at a concentration of 60 µg HA antigen per mL.

Subject analysis set title	CSL425 (15 mcg) Cohort A
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 6 months to less than 3 years received two doses of CSL425 (15 mcg of haemagglutinin antigen per 0.25 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	CSL425 (30 mcg) Cohort A
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 6 months to less than 3 years received two doses of CSL425 (30 mcg of haemagglutinin antigen per 0.5 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	CSL425 (15 mcg) Cohort B
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 3 years to less than 9 years received two doses of CSL425 (15 mcg of haemagglutinin antigen per 0.25 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	CSL425 (30 mcg) Cohort B
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged 3 years to less than 9 years received two doses of CSL425 (30 mcg of haemagglutinin antigen per 0.5 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Subject analysis set title	Total of all reporting groups
Subject analysis set type	Per protocol

Subject analysis set description:

Total of all reporting groups.

Primary: Haemagglutination Inhibition (HI) Antibody Titre Seroconversion Rate After the First Vaccination.

End point title	Haemagglutination Inhibition (HI) Antibody Titre Seroconversion Rate After the First Vaccination.[1]

End point description:

HI antibody titre seroconversion was defined as participants with a pre-vaccination titre of less than 1:10 achieving a post-vaccination HI antibody titre of 1:40 or more; or participants with a pre-vaccination HI titre of 1:10 or more achieving a four-fold or greater increase in post-vaccination HI titre. The Evaluable Population (for the first vaccination) comprised all randomised participants who received the first study vaccination; provided both pre- and post-vaccination blood samples; were not excluded from analyses (eg, for the use of a prohibited medication or a laboratory-confirmed 2009 H1N1 infection between Visit 1 and Visit 3).

End point type	Primary

End point timeframe:

Before and 21 days after the first vaccination

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: Data were analysed using descriptive statistics only.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	76	73	98	99
Units: percentage of participants				
arithmetic mean (confidence interval 95%)	88.2 (78.7 to 94.4)	97.3 (90.5 to 99.7)	85.7 (77.2 to 92)	91.9 (84.7 to 96.4)

Statistical analyses

No statistical analyses for this end point

Primary: HI Antibody Titre Seroconversion Rate After the Second Vaccination

End point title	HI Antibody Titre Seroconversion Rate After the Second Vaccination[2]

End point description:

HI antibody titre seroconversion was defined as participants with a pre-vaccination titre of less than 1:10 achieving a post-vaccination HI antibody titre of 1:40 or more; or participants with a pre-vaccination HI titre of 1:10 or more achieving a four-fold or greater increase in post-vaccination HI titre. The Evaluable Population (for the second vaccination) comprised all randomised participants who received the second study vaccination; provided both pre- and post-vaccination blood samples; were not excluded from analyses (eg, for the use of a prohibited medication or a laboratory-confirmed 2009 H1N1 infection between Visit 1 and Visit 3). The Evaluable Population (for the second vaccination) comprised all randomised participants who received the second study vaccination; provided both pre- and post-vaccination blood samples; were not excluded from analyses (eg, for the use of a prohibited medication or a laboratory-confirmed 2009 H1N1 infection between Visit 1 and Visit 3).

End point type	Primary

End point timeframe:

Before and 21 days after the second vaccination.

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: Data were analysed using descriptive statistics only.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	69	95	96
Units: percentage of participants				
arithmetic mean (confidence interval 95%)	96.9 (89.2 to 99.6)	98.6 (92.2 to 100)	97.9 (92.6 to 99.7)	96.9 (91.1 to 99.4)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Increase (GMFI) in the HI Antibody Titre After the First Vaccination

End point title	Geometric Mean Fold Increase (GMFI) in the HI Antibody Titre After the First Vaccination[3]

End point description:

GMFI in HI antibody titre was defined as the geometric mean of the fold increase in the post-vaccination antibody titre over the pre-vaccination antibody titre.
The Evaluable Population (for the first vaccination) comprised all randomised participants who received the first study vaccination; provided both pre- and post-vaccination blood samples; were not excluded from analyses (eg, for the use of a prohibited medication or a laboratory-confirmed 2009 H1N1 infection between Visit 1 and Visit 3).

End point type	Primary

End point timeframe:

Before and 21 days after the first vaccination.

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: Data were analysed using descriptive statistics only.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	76	73	98	99
Units: geometric mean fold increase				
geometric mean (confidence interval 95%)	13.95 (11.39 to 17.09)	22.17 (17.87 to 27.49)	13.25 (10.84 to 16.19)	15.93 (12.87 to 19.71)

Statistical analyses

No statistical analyses for this end point

Primary: GMFI in the HI Antibody Titre After the Second Vaccination

End point title	GMFI in the HI Antibody Titre After the Second Vaccination[4]

End point description:

GMFI in HI antibody titre was defined as the geometric mean of the fold increase in the post-vaccination antibody titre over the pre-vaccination antibody titre.
The Evaluable Population (for the second vaccination) comprised all randomised participants who received the second study vaccination; provided both pre- and post-vaccination blood samples; were not excluded from analyses (eg, for the use of a prohibited medication or a laboratory-confirmed 2009 H1N1 infection between Visit 1 and Visit 3).

End point type	Primary

End point timeframe:

Before and 21 days after the second vaccination.

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: Data were analysed using descriptive statistics only.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	69	95	96
Units: geometric mean fold increase				
geometric mean (confidence interval 95%)	57.64 (42.87 to 77.5)	72.93 (56.1 to 94.8)	37.48 (28.33 to 49.58)	37.06 (28.77 to 47.75)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving a HI Antibody Titre of 1:40 or More After the First Vaccination

End point title	Percentage of Participants Achieving a HI Antibody Titre of 1:40 or More After the First Vaccination[5]

End point description:

The Evaluable Population (for the first vaccination) comprised all randomised participants who received the first study vaccination; provided both pre- and post-vaccination blood samples; were not excluded from analyses (eg, for the use of a prohibited medication or a laboratory-confirmed 2009 H1N1 infection between Visit 1 and Visit 3).

End point type	Primary

End point timeframe:

21 days after the first vaccination

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: Data were analysed using descriptive statistics only.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	76	73	98	99
Units: percentage of participants				
number (confidence interval 95%)	92.1 (83.6 to 97)	100 (95.1 to 100)	92.9 (85.8 to 97.1)	96 (90 to 98.9)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Achieving a HI Antibody Titre of 1:40 or More After the Second Vaccination

End point title	Percentage of Participants Achieving a HI Antibody Titre of 1:40 or More After the Second Vaccination[6]

End point description:

The Evaluable Population (for the second vaccination) comprised all randomised participants who received the second study vaccination; provided both pre- and post-vaccination blood samples; were not excluded from analyses (eg, for the use of a prohibited medication or a laboratory-confirmed 2009 H1N1 infection between Visit 1 and Visit 3).

End point type	Primary

End point timeframe:

21 days after the 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: Data were analysed using descriptive statistics only.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	64	69	95	96
Units: percentage of participants				
number (confidence interval 95%)	100 (94.4 to 100)	100 (94.8 to 100)	100 (96.2 to 100)	100 (96.2 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency and Intensity of Solicited Adverse Events (AEs) After the First or Second Vaccination - PART A

End point title	Frequency and Intensity of Solicited Adverse Events (AEs) After the First or Second Vaccination - PART A

End point description:

Solicited AEs included AEs that were specifically sought for. Grade 3 solicited AE definitions: Cried when limb was moved/spontaneously painful (Cohort A) or prevented normal daily activities (Cohort B) for injection site pain; Size > 100 mm for injection site redness and induration/swelling; Temperature > 103.1°F (39.5°C) for fevers; Prevented normal daily activities or required medical intervention for all other systemic AEs.
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.
Headache, muscle ache and malaise not solicited for Cohort A.
Appetite and irritability not solicited for Cohort B.

End point type	Secondary

End point timeframe:

During the 7 days after each vaccination.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	80		
Units: percentage of participants				
number (not applicable)				
Any solicited local AE	69.5	63.8		
Any pain at injection site	48.8	43.8		
Grade 3 pain at injection site	1.2	1.3		
Any redness at injection site	53.7	38.8		
Grade 3 redness at injection site	0	1.3		
Any swelling/induration at injection site	30.5	32.5		
Grade 3 swelling/induration at injection site	0	2.5		

Any solicited systemic AE	79.3	93.8		
Any nausea/vomiting	13.4	30		
Grade 3 nausea/vomiting	1.2	1.3		
Any diarrhoea	26.8	32.5		
Grade 3 diarrhoea	1.2	0		
Any loss of appetite	40.2	50		
Grade 3 loss of appetite	1.2	0		
Any irritability	63.4	72.5		
Grade 3 irritability	2.4	1.3		
Any fever	50	71.3		
Grade 3 fever	1.2	8.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency and Intensity of Solicited Adverse Events (AEs) After the First or Second Vaccination - PART B

End point title	Frequency and Intensity of Solicited Adverse Events (AEs) After the First or Second Vaccination - PART B

End point description:

Solicited AEs included AEs that were specifically sought for. Grade 3 solicited AE definitions: Cried when limb was moved/spontaneously painful (Cohort A) or prevented normal daily activities (Cohort B) for injection site pain; Size > 100 mm for injection site redness and induration/swelling; Temperature > 103.1°F (39.5°C) for fevers; Prevented normal daily activities or required medical intervention for all other systemic AEs.
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.
Appetite and irritability not solicited for in Cohort B.
Headache, muscle ache and malaise not solicited for in Cohort A.

End point type	Secondary

End point timeframe:

During the 7 days after each vaccination.

End point values	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	103	104		
Units: percentage of participants				
number (not applicable)				
Any solicited local AE	68	71.2		
Any pain at injection site	59.2	64.4		
Grade 3 pain at injection site	0	1		
Any redness at injection site	37.9	37.5		
Grade 3 redness at injection site	2.9	2.9		
Any swelling/induration at injection site	25.2	26.9		
Grade 3 swelling/induration at injection site	0	4.8		
Any solicited systemic AE	54.4	61.5		

Any nausea/vomiting	15.5	20.2		
Grade 3 nausea/vomiting	0	1		
Any diarrhoea	12.6	12.5		
Grade 3 diarrhoea	0	0		
Any fever	20.4	29.8		
Grade 3 fever	0	2.9		
Any headache	27.2	23.1		
Grade 3 headache	0	1		
Any muscle ache	15.5	22.1		
Grade 3 muscle ache	0	1		
Any malaise	19.4	26.9		
Grade 3 malaise	0	1.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Solicited AEs After the First Vaccination - PART A

End point title	Duration of Solicited AEs After the First Vaccination - PART A

End point description:

Solicited AEs included AEs that were specifically sought for.
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.
Headache, muscle ache and malaise not solicited for in Cohort A.

End point type	Secondary

End point timeframe:

During the 7 days after the first vaccination and up to Day 20 after the first vaccination if AE is ongoing at Day 7.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	82	80		
Units: days				
arithmetic mean (standard deviation)				
Pain at injection site	1.48 (± 0.677)	1.52 (± 0.823)		
Redness at injection site	2.08 (± 1.382)	2.23 (± 1.602)		
Swelling/induration at injection site	1.88 (± 0.957)	1.64 (± 0.745)		
Nausea/vomiting	1.33 (± 0.5)	1.05 (± 0.213)		
Diarrhoea	1.67 (± 1.328)	1.55 (± 0.945)		
Loss of appetite	2.32 (± 1.906)	1.97 (± 1.447)		
Irritability	1.78 (± 1.56)	1.73 (± 1.574)		
Fever	1.77 (± 1.547)	1.52 (± 1.079)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Solicited AEs After the First Vaccination - PART B

End point title	Duration of Solicited AEs After the First Vaccination - PART B

End point description:

Solicited AEs included AEs that were specifically sought for.
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.
Loss of appetite and irritability not solicited for in Cohort B.

End point type	Secondary

End point timeframe:

During the 7 days after the first vaccination and up to Day 20 after the first vaccination if AE is ongoing at Day 7.

End point values	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	103	104		
Units: days				
arithmetic mean (standard deviation)				
Pain at injection site	1.91 (± 1.221)	1.8 (± 1.016)		
Redness at injection site	2.26 (± 1.347)	2 (± 1.134)		
Swelling/induration at injection site	1.6 (± 0.737)	2.04 (± 1.136)		
Nausea/vomiting	1.18 (± 0.405)	1.53 (± 1.837)		
Diarrhoea	1.11 (± 0.333)	1.17 (± 0.577)		
Fever	1.4 (± 0.737)	1.54 (± 1.319)		
Headache	2.04 (± 2.911)	1.63 (± 1.149)		
Muscle ache	1.45 (± 0.6888)	1.86 (± 2.175)		
Malaise	1.6 (± 0.91)	1.69 (± 1.966)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Solicited AEs After the Second Vaccination - PART A

End point title	Duration of Solicited AEs After the Second Vaccination - PART A

End point description:

Solicited AEs included AEs that were specifically sought for.
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.
Headache, muscle ache and malaise not solicited for in Cohort A.

End point type	Secondary

End point timeframe:

During the 7 days after the second vaccination and up to Day 20 after the second vaccination if AE was ongoing at Day 7.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	71		
Units: days				
arithmetic mean (standard deviation)				
Pain at injection site	1.67 (± 0.966)	1.64 (± 1.002)		
Redness at injection site	1.69 (± 1.004)	2.14 (± 1.037)		
Swelling/induration at injection site	1.74 (± 0.872)	2.32 (± 1.108)		
Nausea/vomiting	5 (± 8.832)	1 (± 0)		
Diarrhoea	3.4 (± 3.777)	1.25 (± 0.452)		
Loss of appetite	3.15 (± 4.475)	1.73 (± 0.883)		
Irritability	2.57 (± 2.41)	2.1 (± 1.533)		
Fever	2.14 (± 3.005)	1.63 (± 1.165)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Solicited AEs After the Second Vaccination - PART B

End point title	Duration of Solicited AEs After the Second Vaccination - PART B

End point description:

Solicited AEs included AEs that were specifically sought for.
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.
Loss of appetite and irritability not solicited for in Cohort B.

End point type	Secondary

End point timeframe:

During the 7 days after the second vaccination and up to Day 20 after the second vaccination if AE was ongoing at Day 7.

End point values	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	100	99		
Units: days				
arithmetic mean (standard deviation)				
Pain at injection site	1.9 (± 1.179)	1.8 (± 1.04)		
Redness at injection site	1.92 (± 1.055)	1.7 (± 0.822)		
Swelling/induration at injection site	2.24 (± 1.348)	2.27 (± 1.751)		
Nausea/vomiting	1.43 (± 0.787)	1.11 (± 0.333)		
Diarrhoea	1.4 (± 0.894)	2 (± 1)		
Fever	1.54 (± 0.877)	1.67 (± 1.414)		
Headache	1.33 (± 0.686)	1.73 (± 2.412)		

Muscle ache	1.6 (± 0.516)	1.29 (± 0.756)		
Malaise	1.2 (± 0.422)	2 (± 1.826)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Serious Adverse Events (SAEs), Adverse Events of Special Interest (AESIs), and New Onset of Chronic Illnesses (NOCIs)

End point title	Incidence of Serious Adverse Events (SAEs), Adverse Events of Special Interest (AESIs), and New Onset of Chronic Illnesses (NOCIs)

End point description:

An AESI was defined as an AE for which the association with seasonal influenza vaccine was unclear. A NOCI was defined as the diagnosis of a new medical condition that was chronic in nature, including those potentially controllable by medication (eg, diabetes, asthma).
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.

End point type	Secondary

End point timeframe:

Up to 180 days after the last vaccination.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	82	80	103	104
Units: percentage of participants				
number (not applicable)				
At least one SAE	4.9	1.3	1	1
Related SAE	0	0	0	1
At least one AESI	2.4	1.3	0	0
Related AESI	0	0	0	0
At least one NOCI	1.2	3.8	1.9	0
Related NOCI	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency and Intensity of Unsolicited Adverse Events After the First or Second Vaccination

End point title	Frequency and Intensity of Unsolicited Adverse Events After the First or Second Vaccination

End point description:

Unsolicited AEs included AEs other than those specifically sought for. Grade 1 unsolicited AE definition: Easily tolerated and did not interfere with normal daily activities. Grade 2 unsolicited AE definition:

Some interference with normal daily activities. Grade 3 unsolicited AE definition: Prevented normal daily activities.
The Safety Population comprised all participants who received at least one dose of the vaccine and provided follow-up safety data.

End point type	Secondary

End point timeframe:

During the 21 days after each vaccination; up to 180 days after the last vaccination for SAEs, AESIs, and NOCIs.

End point values	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B	CSL425 (30 mcg) Cohort B
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	82	80	103	104
Units: percentage of subjects				
number (not applicable)				
At least one unsolicited AE	78	82.5	67	76
Grade 1 unsolicited AE	26.8	33.8	27.2	37.5
Grade 2 unsolicited AE	41.5	41.3	37.9	26.9
Grade 3 unsolicited AE	9.8	7.5	1.9	11.5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For SAEs: up to 180 days after the last vaccination. For Other AEs: solicited AEs: during the 7 days after each vaccination; unsolicited AEs: during the 21 days after each vaccination; up to 180 days after the last vaccination for AESIs and NOCIs.

Adverse event reporting additional description:

Loss of appetite and irritability were not solicited for in Cohort B.
Headache, muscle ache and malaise were not solicted for in Cohort A.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13

Reporting groups

Reporting group title	CSL425 (15 mcg) Cohort A

Reporting group description:

Participants aged 6 months to less than 3 years received two doses of CSL425 (15 mcg of haemagglutinin antigen per 0.25 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Reporting group title	CSL425 (30 mcg) Cohort A

Reporting group description:

Participants aged 6 months to less than 3 years received two doses of CSL425 (30 mcg of haemagglutinin antigen per 0.5 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Reporting group title	CSL425 (15 mcg) Cohort B

Reporting group description:

Participants aged 3 years to less than 9 years received two doses of CSL425 (15 mcg of haemagglutinin antigen per 0.25 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Reporting group title	CSL425 (30 mcg) Cohort B

Reporting group description:

Participants aged 3 years to less than 9 years received two doses of CSL425 (30 mcg of haemagglutinin antigen per 0.5 mL dose) by intramuscular injection into the deltoid region of the arm on Day 0 and Day 21.

Serious adverse events	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 82 (4.88%)	1 / 80 (1.25%)	1 / 103 (0.97%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	0 / 82 (0.00%)	1 / 80 (1.25%)	0 / 103 (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
Nervous system disorders			

Convulsion in childhood			
subjects affected / exposed	2 / 82 (2.44%)	0 / 80 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 80 (0.00%)	0 / 103 (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
Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: defined as a NOCI.		
subjects affected / exposed	1 / 82 (1.22%)	1 / 80 (1.25%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 82 (1.22%)	0 / 80 (0.00%)	0 / 103 (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
Lobar pneumonia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 80 (0.00%)	1 / 103 (0.97%)
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	CSL425 (30 mcg) Cohort B		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 104 (0.96%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Convulsion in childhood			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: defined as a NOCI.		
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lobar pneumonia			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CSL425 (15 mcg) Cohort A	CSL425 (30 mcg) Cohort A	CSL425 (15 mcg) Cohort B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	81 / 82 (98.78%)	78 / 80 (97.50%)	91 / 103 (88.35%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 82 (3.66%)	6 / 80 (7.50%)	4 / 103 (3.88%)
occurrences (all)	3	6	5
Excoriation			

subjects affected / exposed	2 / 82 (2.44%)	1 / 80 (1.25%)	3 / 103 (2.91%)
occurrences (all)	2	1	3
Contusion			
subjects affected / exposed	1 / 82 (1.22%)	1 / 80 (1.25%)	0 / 103 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	12 / 82 (14.63%)	10 / 80 (12.50%)	7 / 103 (6.80%)
occurrences (all)	14	10	8
Pyrexia			
subjects affected / exposed	10 / 82 (12.20%)	4 / 80 (5.00%)	3 / 103 (2.91%)
occurrences (all)	10	4	4
Pain at Injection Site			
subjects affected / exposed	40 / 82 (48.78%)	35 / 80 (43.75%)	61 / 103 (59.22%)
occurrences (all)	52	47	96
Redness at Injection Site			
subjects affected / exposed	44 / 82 (53.66%)	31 / 80 (38.75%)	39 / 103 (37.86%)
occurrences (all)	66	44	53
Swelling/Induration at Injection Site			
subjects affected / exposed	25 / 82 (30.49%)	26 / 80 (32.50%)	26 / 103 (25.24%)
occurrences (all)	35	33	32
Nausea/Vomiting			
subjects affected / exposed	11 / 82 (13.41%)	24 / 80 (30.00%)	16 / 103 (15.53%)
occurrences (all)	15	26	18
Diarrhoea			
subjects affected / exposed	22 / 82 (26.83%)	26 / 80 (32.50%)	13 / 103 (12.62%)
occurrences (all)	28	32	14
Loss of appetite			
subjects affected / exposed	33 / 82 (40.24%)	40 / 80 (50.00%)	0 / 103 (0.00%)
occurrences (all)	48	55	0
Irritability			
subjects affected / exposed	52 / 82 (63.41%)	58 / 80 (72.50%)	0 / 103 (0.00%)
occurrences (all)	92	99	0
Fever			

subjects affected / exposed	41 / 82 (50.00%)	57 / 80 (71.25%)	21 / 103 (20.39%)
occurrences (all)	51	75	28
Headache			
subjects affected / exposed	0 / 82 (0.00%)	0 / 80 (0.00%)	28 / 103 (27.18%)
occurrences (all)	0	0	42
Muscle ache (Myalgia)			
subjects affected / exposed	0 / 82 (0.00%)	0 / 80 (0.00%)	16 / 103 (15.53%)
occurrences (all)	0	0	21
Malaise			
subjects affected / exposed	0 / 82 (0.00%)	0 / 80 (0.00%)	20 / 103 (19.42%)
occurrences (all)	0	0	25
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 82 (0.00%)	2 / 80 (2.50%)	8 / 103 (7.77%)
occurrences (all)	0	2	8
Gastrointestinal disorders			
Teething			
subjects affected / exposed	14 / 82 (17.07%)	12 / 80 (15.00%)	0 / 103 (0.00%)
occurrences (all)	18	19	0
Vomiting			
subjects affected / exposed	0 / 82 (0.00%)	4 / 80 (5.00%)	2 / 103 (1.94%)
occurrences (all)	0	4	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 82 (7.32%)	11 / 80 (13.75%)	13 / 103 (12.62%)
occurrences (all)	6	12	13
Rhinorrhoea			
subjects affected / exposed	8 / 82 (9.76%)	17 / 80 (21.25%)	4 / 103 (3.88%)
occurrences (all)	8	17	4
Asthma			
subjects affected / exposed	2 / 82 (2.44%)	4 / 80 (5.00%)	3 / 103 (2.91%)
occurrences (all)	2	4	4
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 82 (8.54%)	3 / 80 (3.75%)	0 / 103 (0.00%)
occurrences (all)	7	3	0

Dermatitis diaper			
subjects affected / exposed	7 / 82 (8.54%)	1 / 80 (1.25%)	0 / 103 (0.00%)
occurrences (all)	7	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	22 / 82 (26.83%)	28 / 80 (35.00%)	22 / 103 (21.36%)
occurrences (all)	28	31	26
Viral infection			
subjects affected / exposed	4 / 82 (4.88%)	0 / 80 (0.00%)	3 / 103 (2.91%)
occurrences (all)	4	0	4

Non-serious adverse events	CSL425 (30 mcg) Cohort B		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 104 (92.31%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	7 / 104 (6.73%)		
occurrences (all)	7		
Excoriation			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences (all)	8		
Contusion			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences (all)	6		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	9 / 104 (8.65%)		
occurrences (all)	9		
Pyrexia			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Pain at Injection Site			
subjects affected / exposed	67 / 104 (64.42%)		
occurrences (all)	105		
Redness at Injection Site			

subjects affected / exposed	39 / 104 (37.50%)		
occurrences (all)	52		
Swelling/Induration at Injection Site			
subjects affected / exposed	28 / 104 (26.92%)		
occurrences (all)	40		
Nausea/Vomiting			
subjects affected / exposed	21 / 104 (20.19%)		
occurrences (all)	28		
Diarrhoea			
subjects affected / exposed	13 / 104 (12.50%)		
occurrences (all)	15		
Loss of appetite			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Fever			
subjects affected / exposed	31 / 104 (29.81%)		
occurrences (all)	37		
Headache			
subjects affected / exposed	24 / 104 (23.08%)		
occurrences (all)	38		
Muscle ache (Myalgia)			
subjects affected / exposed	23 / 104 (22.12%)		
occurrences (all)	28		
Malaise			
subjects affected / exposed	28 / 104 (26.92%)		
occurrences (all)	39		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	4 / 104 (3.85%)		
occurrences (all)	5		
Gastrointestinal disorders			
Teething			

subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 104 (10.58%)		
occurrences (all)	12		
Rhinorrhoea			
subjects affected / exposed	8 / 104 (7.69%)		
occurrences (all)	10		
Asthma			
subjects affected / exposed	3 / 104 (2.88%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Dermatitis diaper			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	24 / 104 (23.08%)		
occurrences (all)	26		
Viral infection			
subjects affected / exposed	9 / 104 (8.65%)		
occurrences (all)	9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2009	The purpose of the first protocol amendment was to make the following revisions to the protocol: To incorporate changes to the exclusion criteria. Exclusion criteria were updated to exclude - Participants with a laboratory-confirmed infection with untyped influenza A since May 2009. - Participants who were receiving immunosuppressive or immunomodulative therapy, or have received such therapy within the 3 months preceding study entry. - To update the list of prohibited medications to include immunosuppressive or immunomodulative therapy.
01 October 2009	The purpose of the second protocol amendment was to make the following revisions to the protocol: - In order to aid public health decision-making regarding a potential 2009 H1N1 influenza vaccine immunisation program, the randomisation code will be unblinded after all enrolled participants complete the Active Study Period and the data collected during the Active Study Period are entered into the database. This modification altered the study design from a randomised, observer-blind, parallel group study to a randomised, observer-blind parallel group study with an open-label follow-up study period. - To clarify the tertiary analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
31 August 2009	Halting rules were triggered once because of a suspected unexpected serious adverse reaction (SUSAR) of pyrexia reported in an 8-year old participant in the 30 µg group. After medical review, the DSMB recommenced the study.	01 September 2009

Notes:

Limitations and caveats

None reported