Clinical trial results:
An Observer-Blind, Randomized, Comparator-Controlled, Single-Centre Study to Evaluate the Tolerability, Safety, and Immunogenicity of Inactivated Influenza Vaccine, CSL Limited in a Healthy Pediatrics and Adult Population (aged >=3 years to <= 80 years)

Summary

EudraCT number	2015-000177-12
Trial protocol	Outside EU/EEA
Global end of trial date	20 June 2007

Results information

Result version number	v1 (current)
This version publication date	03 August 2016
First version publication date	03 August 2016

Trial information

Trial identification

Sponsor protocol code	CSLCT-CHF-06-25

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CSL Ltd
Sponsor organisation address	45 Poplar Rd, Parkville, Australia, 3052
Public contact	Clinical Program Director, Seqirus, SeqirusAU.ClinicalTrials@seqirus.com
Scientific contact	Clinical Program Director, Seqirus, SeqirusAU.ClinicalTrials@seqirus.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	26 September 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 June 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of CSL Inactivated Influenza Virus Vaccine in a healthy paediatric, adult and senior adult population (=>3 years to =< 80 years of age).

Protection of trial subjects:

The relevant documents including the trial protocol and informed consent form passed review of a Chinese based independent ethical committee on May 10, 2007.
This study was conducted in accordance with SFDA requirements and GCP/Declaration of Helsinki principles.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 May 2007
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	China: 720
Worldwide total number of subjects	720
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)	0
Children (2-11 years)	70
Adolescents (12-17 years)	200
Adults (18-64 years)	300
From 65 to 84 years	150
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

720 volunteers were recruited into the study. The study was conducted in Guangxi, China.

Pre-assignment

Screening details:

Phase I component: 30 subjects aged 3 - 80 years administered Fluvax.
Phase III component: 690 subjects. The CRO prepared the study randomization code at a 2:1 ratio of the Fluvax test vaccine : Fluarix comparator vaccine.

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

Blinding implementation details:

The clinical trial was divided into two stages: Phase I and Phase III.
Phase I: Only investigational vaccine (Fluvax) was administered. The design was an open design, without a comparator arm, for the purpose of observing adverse reactions (there was no immunogenicity component).
Phase III: An observer blinded, randomized and parallel control trial to compare both safety and immunogenicity between CSL influenza vaccine (Fluvax) and a comparator influenza vaccine (Fluarix).

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase I (Fluvax)

Arm description:

For the phase I component, Fluvax vaccine was administered to eligible volunteers. The phase was an open design without the use of a comparator arm.

Arm type	Experimental
Investigational medicinal product name	Fluvax (Inactivated split virus influenza vaccine for injection)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Fluvax - Inactivated split virus influenza vaccine for injection (containing H1N1, H3N2 and B strains)
Manufacturer: CSL Ltd.
A 0.5 mL dose was administered.

Arm title	Phase III (Fluvax)

Arm description:

Subjects were administered the CSL Fluvax vaccine. All subjects completed one vaccine injection and provided their safety data. All of these subjects were included in the safety analysis set.

Arm type	Experimental
Investigational medicinal product name	Fluvax (Inactivated split virus influenza vaccine for injection)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Fluvax - Inactivated split virus influenza vaccine for injection (containing H1N1, H3N2 and B strains)
Manufacturer: CSL Ltd.

A 0.5 mL dose was administered.

Arm title	Phase III (Comparator)

Arm description:

Subjects were administered the comparator influenza vaccine (Fluarix). All subjects completed one vaccine injection and provided their safety data. All of these subjects were included in the safety analysis set.

Arm type	Active comparator
Investigational medicinal product name	Fluarix (Inactivated split virus influenza vaccine for injection)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Comparator vaccine: Inactivated split virus influenza vaccine (Fluarix) for injection (containing the H1N1, H3N2 and B strains).
Manufacturer: Shanghai GSK Biological Ltd.
A 0.5 mL dose was administered.

Number of subjects in period 1	Phase I (Fluvax)	Phase III (Fluvax)	Phase III (Comparator)
Started	30	460	230
Completed	30	460	230

Baseline characteristics

Reporting groups	
Reporting group title	Phase I (Fluvax)
Reporting group description:	
For the phase I component, Fluvax vaccine was administered to eligible volunteers. The phase was an open design without the use of a comparator arm.	
Reporting group title	Phase III (Fluvax)
Reporting group description:	
Subjects were administered the CSL Fluvax vaccine. All subjects completed one vaccine injection and provided their safety data. All of these subjects were included in the safety analysis set.	
Reporting group title	Phase III (Comparator)
Reporting group description:	
Subjects were administered the comparator influenza vaccine (Fluarix). All subjects completed one vaccine injection and provided their safety data. All of these subjects were included in the safety analysis set.	

Reporting group values	Phase I (Fluvax)	Phase III (Fluvax)	Phase III (Comparator)
Number of subjects	30	460	230
Age categorical			
Pediatric: age >= 3 years and < 16 years Adultage >= 16 years and < 60 years Elderlyage >= 60 years and <= 80 years			
Units: Subjects			
Pediatric	10	184	92
Adult	12	184	92
Elderly	8	92	46
Gender categorical			
Note: Gender data were not available for the Phase I component of the trial and have been presented as an equal number of males and females.			
Units: Subjects			
Female	15	282	141
Male	15	178	89

Reporting group values	Total		
Number of subjects	720		
Age categorical			
Pediatric: age >= 3 years and < 16 years Adultage >= 16 years and < 60 years Elderlyage >= 60 years and <= 80 years			
Units: Subjects			
Pediatric	286		
Adult	288		
Elderly	146		
Gender categorical			
Note: Gender data were not available for the Phase I component of the trial and have been presented as an equal number of males and females.			
Units: Subjects			
Female	438		
Male	282		

End points

End points reporting groups

Reporting group title	Phase I (Fluvax)

Reporting group description:

For the phase I component, Fluvax vaccine was administered to eligible volunteers. The phase was an open design without the use of a comparator arm.

Reporting group title	Phase III (Fluvax)

Reporting group description:

Subjects were administered the CSL Fluvax vaccine. All subjects completed one vaccine injection and provided their safety data. All of these subjects were included in the safety analysis set.

Reporting group title	Phase III (Comparator)

Reporting group description:

Subjects were administered the comparator influenza vaccine (Fluarix). All subjects completed one vaccine injection and provided their safety data. All of these subjects were included in the safety analysis set.

Subject analysis set title	CSL Vaccine - immunogenicity
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects who were enrolled into the phase III component, were vaccinated with CSL vaccine, and provided a blood sample before and after vaccination, were included in the immunogenicity per protocol set.

Subject analysis set title	Comparator Vaccine - immunogenicity
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects who were enrolled into the phase III component, were vaccinated with comparator vaccine, and provided a blood sample before and after vaccination, were included in the immunogenicity per protocol set.

Primary: Phase I: Tolerability observation of the CSL vaccine

End point title	Phase I: Tolerability observation of the CSL vaccine[1][2]

End point description:

End point type	Primary

End point timeframe:

Collection of solicited local and systemic adverse reactions within 72 hours after vaccination.
Collection of any unsolicited adverse reactions from day 4 to day 28 after 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: Statistical analysis data are not available for this section.

[2] - 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: Data captured for this end point are only for subjects in the phase I component of the trial.

End point values	Phase I (Fluvax)			
Subject group type	Reporting group			
Number of subjects analysed	30[3]			
Units: Subjects reporting event				
Local reaction - mild pain	4			
Local reaction - mild erythema	1			
Local reaction - mild induration	1			
Local reaction - mild ecchymosis	1			

Systemic reaction - mild myalgia	1			
Systemic reaction - mild fatigue	1			

Notes:

[3] - Number of subjects reporting an Adverse Event (AE). One subject had 4 AEs; 5 subjects had 1 AE each.

Statistical analyses

No statistical analyses for this end point

Primary: Phase III: Assessment of solicited fever events

End point title	Phase III: Assessment of solicited fever events[4][5]

End point description:

End point type	Primary

End point timeframe:

Within 72 hours after 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: Statistical analysis data are not available for this section.

[5] - 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: Data captured for this end point are only for subjects in the phase III component of the trial.

End point values	Phase III (Fluvax)	Phase III (Comparator)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	460	230		
Units: Subjects reporting event				
Systemic reaction – fever, mild (paediatric)	3	3		
Systemic reaction – fever, mild (adult)	7	4		
Systemic reaction – fever, mild (elderly)	6	4		
Systemic reaction – fever, mild (overall)	16	11		
Systemic reaction – fever, moderate (paediatric)	2	0		
Systemic reaction – fever, moderate (adult)	1	0		
Systemic reaction – fever, moderate (elderly)	0	1		
Systemic reaction – fever, moderate (overall)	3	1		
Systemic reaction – fever, total (overall)	19	12		

Statistical analyses

No statistical analyses for this end point

Primary: Phase III: Other solicited adverse events

End point title	Phase III: Other solicited adverse events[6][7]

End point description:

Overall number of subjects reporting solicited adverse events (other than fever), both systemic and local, for the phase III component of the trial.

End point type	Primary

End point timeframe:

Up to 28 days after 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: Statistical analysis data are not available for this section.

[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: Data captured for this end point are only for subjects in the phase III component of the trial.

End point values	Phase III (Fluvax)	Phase III (Comparator)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	460	230		
Units: number of subjects				
arthralgia	2	0		
myalgia	2	0		
fatigue	4	0		
headache	2	0		
dizziness	6	0		
low back pain	1	0		
erythemia	2	1		
pain	9	2		
induration	2	1		
swelling	6	3		
ecchymosis	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion

End point title	Seroconversion

End point description:

The overall number of phase III subjects (in the immunogenicity per protocol population) achieving seroconversion is listed for each influenza strain (H1N1, H3N2 and B strains) included in the vaccine.

End point type	Secondary

End point timeframe:

21 days after vaccination

End point values	CSL Vaccine - immunogenicity	Comparator Vaccine - immunogenicity		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	403	207		
Units: number of subjects				
Total - H1N1 strain	355	189		
Total - H3N2 strain	310	170		
Total - B strain	331	159		

Statistical analyses

No statistical analyses for this end point

Secondary: Seroprotection

End point title	Seroprotection

End point description:

The overall number of phase III subjects (in the immunogenicity per protocol population) achieving seroprotection are listed for each influenza strain (H1N1, H3N2 and B strains) included in the vaccine.

End point type	Secondary

End point timeframe:

21 days after vaccination

End point values	CSL Vaccine - immunogenicity	Comparator Vaccine - immunogenicity		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	403	207		
Units: number of subject				
Total - H1N1 strain	400	200		
Total - H3N2 strain	392	205		
Total - B strain	372	183		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titre

End point title	Geometric Mean Titre

End point description:

The pre- and post- vaccination haemagglutinin assay Geometric Mean Titres for the phase III subjects (in the immunogenicity per protocol population) are listed for each influenza strain (H1N1, H3N2 and B strains) included in the vaccine.

End point type	Secondary

End point timeframe:
21 days after vaccination

End point values	CSL Vaccine - immunogenicity	Comparator Vaccine - immunogenicity		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	403	207		
Units: Titre (GMT)				
Total - H1N1 strain (pre-vaccine)	44	38		
Total - H1N1 strain (post-vaccine)	545	775		
Total - H3N2 strain (pre-vaccine)	42	42		
Total - H3N2 strain (post-vaccine)	458	671		
Total - B strain (pre-vaccine)	14	13		
Total - B strain (post-vaccine)	167	129		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Within 28 days after vaccination

Assessment type	Systematic

Dictionary used

Dictionary name	Not available
Dictionary version	0

Reporting groups

Reporting group title	Safety population

Reporting group description:

Available adverse event data are presented as end point analyses and are not able to be fully reported in this section. There were no serious adverse events reported in this trial.

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 720 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 720 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The number of subjects experiencing an adverse event is presented as part of the primary end point data set in the end point section. The number of adverse events experienced by the subjects is not available.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Limited data are available for this trial affecting data entry as noted throughout. Estimated numbers have been entered for the Trial Information 'Age group breakdown for trial' section; actual numbers are provided in the Age Characteristics section.

Notes: