



## 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 $\geq 3$ years to $\leq 80$ 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,<br>SeqirusAU.ClinicalTrials@seqirus.com |
| Scientific contact           | Clinical Program Director, Seqirus,<br>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:

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**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:

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**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 ( $\geq 3$  years to  $\leq 80$  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:

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**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:

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**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              |
| <b>Arm title</b>             | 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.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | 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.

|   |   |
|---|---|
| <b>Arm title</b>  | Phase III (Comparator)  |
| Arm description:<br>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.

| <b>Number of subjects in period 1</b> | 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:<br>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:<br>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:<br>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 $\geq$ 3 years and $<$ 16 years<br>Adultage $\geq$ 16 years and $<$ 60 years<br>Elderlyage $\geq$ 60 years and $\leq$ 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 $\geq$ 3 years and $<$ 16 years<br>Adultage $\geq$ 16 years and $<$ 60 years<br>Elderlyage $\geq$ 60 years and $\leq$ 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:<br>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:<br>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:<br>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:<br>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:<br>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 <sup>[1][2]</sup> |
| End point description:   |  |
| End point type   | Primary  |
| End point timeframe:<br>Collection of solicited local and systemic adverse reactions within 72 hours after vaccination.<br>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 <sup>[3]</sup> |  |  |  |
| 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 <sup>[4][5]</sup> |
|-----------------|---|

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<br>(Fluvax) | Phase III<br>(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 <sup>[6][7]</sup> |
|-----------------|---|

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<br>(Fluvax) | Phase III<br>(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                         |  |  |
| erythema                    | 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:<br>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:<br>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:<br>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<sup>[1]</sup>

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

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### 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: