



## Clinical trial results:

### Immunogenicity and Safety of the Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation (Intramuscular Route)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2008-000943-33 |
| Trial protocol           | GB             |
| Global end of trial date | 23 July 2008   |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 05 February 2016 |
| First version publication date | 03 December 2014 |

#### Trial information

##### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | GRT83 |
|-----------------------|-------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00718146 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Sanofi Pasteur SA   |
| Sponsor organisation address | 1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280  |
| Public contact               | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 65 66 04, derek.wallace@sanofipasteur.com |
| Scientific contact           | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 65 66 04, derek.wallace@sanofipasteur.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? | No |

Notes:

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**Results analysis stage**

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|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 07 August 2008 |
| Is this the analysis of the primary completion data? | No             |

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|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 23 July 2008 |
| Was the trial ended prematurely? | No           |

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Notes:

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**General information about the trial**

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Main objective of the trial:

To evaluate the compliance, in terms of immunogenicity, of the inactivated, split-virion influenza vaccine Northern Hemisphere 2008-2009 formulation with the requirements of the Committee for Human Medicinal Products (CHMP) Note for Guidance (NfG) CPMP/BWP/214/96.

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Protection of trial subjects:

Only subjects who met all the study inclusion and none of the exclusion criteria were vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

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Background therapy:

Not applicable

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Evidence for comparator:

Not applicable

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|   |              |
|---|--------------|
| Actual start date of recruitment                          | 26 June 2008 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United Kingdom: 130 |
| Worldwide total number of subjects   | 130                 |
| EEA total number of subjects         | 130                 |

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Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 90 |

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|                     |    |
|---------------------|----|
| From 65 to 84 years | 40 |
| 85 years and over   | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Study subjects were enrolled from 26 June 2008 to 23 July 2008 in 2 clinical centers in the United Kingdom.

### Pre-assignment

Screening details:

A total of 130 subjects who met all inclusion criteria and none of the exclusion criteria were enrolled and vaccinated.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

Blinding implementation details:

Not applicable

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | 18 to 60 years |
|------------------|----------------|

Arm description:

Subjects aged 18 to 60 years who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Influenza vaccine (split virion, inactivated) |
| Investigational medicinal product code | 314   |
| Other name                             |   |
| Pharmaceutical forms                   | Suspension for injection                      |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:

0.5 mL, intramuscular, one dose on Day 0.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | 61 years or older |
|------------------|-------------------|

Arm description:

Subjects aged 61 years or older who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Influenza vaccine (split virion, inactivated) |
| Investigational medicinal product code | 314   |
| Other name                             |   |
| Pharmaceutical forms                   | Suspension for injection                      |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:

0.5 mL, intramuscular, one dose on Day 0.

| <b>Number of subjects in period 1</b> | 18 to 60 years | 61 years or older |
|---------------------------------------|----------------|-------------------|
| Started                               | 65             | 65                |
| Completed                             | 65             | 65                |

## Baseline characteristics

### Reporting groups

|   |                   |
|---|-------------------|
| Reporting group title   | 18 to 60 years    |
| Reporting group description:  |                   |
| Subjects aged 18 to 60 years who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0.    |                   |
| Reporting group title   | 61 years or older |
| Reporting group description:  |                   |
| Subjects aged 61 years or older who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0. |                   |

| Reporting group values                             | 18 to 60 years | 61 years or older | Total |
|--|----------------|-------------------|-------|
| Number of subjects                                 | 65             | 65                | 130   |
| Age categorical                                    |                |                   |       |
| Units: Subjects                                    |                |                   |       |
| In utero   | 0              | 0                 | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0              | 0                 | 0     |
| Newborns (0-27 days)                               | 0              | 0                 | 0     |
| Infants and toddlers (28 days-23 months)           | 0              | 0                 | 0     |
| Children (2-11 years)                              | 0              | 0                 | 0     |
| Adolescents (12-17 years)                          | 0              | 0                 | 0     |
| Adults (18-64 years)                               | 65             | 25                | 90    |
| From 65-84 years                                   | 0              | 40                | 40    |
| 85 years and over                                  | 0              | 0                 | 0     |
| Age continuous                                     |                |                   |       |
| Units: years                                       |                |                   |       |
| arithmetic mean                                    | 41.2           | 67.5              |       |
| standard deviation                                 | ± 14.28        | ± 4.24            | -     |
| Gender categorical                                 |                |                   |       |
| Units: Subjects                                    |                |                   |       |
| Female   | 31             | 32                | 63    |
| Male   | 34             | 33                | 67    |
| Previous influenza vaccination                     |                |                   |       |
| Units: Subjects                                    |                |                   |       |
| Yes  | 23             | 47                | 70    |
| No   | 42             | 18                | 60    |
| Previous influenza infection last winter           |                |                   |       |
| Units: Subjects                                    |                |                   |       |
| Yes  | 3              | 1                 | 4     |
| No   | 62             | 64                | 126   |

## End points

### End points reporting groups

|   |                   |
|---|-------------------|
| Reporting group title   | 18 to 60 years    |
| Reporting group description:<br>Subjects aged 18 to 60 years who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0.    |                   |
| Reporting group title   | 61 years or older |
| Reporting group description:<br>Subjects aged 61 years or older who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0. |                   |

### Primary: Summary of Geometric Mean Titers (GMTs) of influenza Vaccine Antibodies Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route

|   |  |
|---|--|
| End point title   | Summary of Geometric Mean Titers (GMTs) of influenza Vaccine Antibodies Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route <sup>[1]</sup> |
| End point description:<br>Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique. |  |
| End point type  | Primary  |
| End point timeframe:<br>Day 0 (pre-vaccination) and Day 21 post 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                              | 18 to 60 years      | 61 years or older   |  |  |
|---|---------------------|---------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                   | 64                  | 65                  |  |  |
| Units: Titers                                 |                     |                     |  |  |
| geometric mean (confidence interval 95%)      |                     |                     |  |  |
| A/Brisbane/59/2007 like strain (H1N1; Day 0)  | 18.1 (13.1 to 25.1) | 26.4 (19.4 to 35.8) |  |  |
| A/Brisbane/10/2007 like strain (H3N2; Day 0)  | 10.8 (8.31 to 14)   | 14.2 (10.3 to 19.7) |  |  |
| B/Florida/4/2006 like strain (B; Day 0)       | 13.5 (10.6 to 17.1) | 23.2 (18.2 to 29.7) |  |  |
| A/Brisbane/59/2007 like strain (H1N1; Day 21) | 311 (235 to 413)    | 127 (96.6 to 166)   |  |  |
| A/Brisbane/10/2007 like strain (H3N2; Day 21) | 144 (97.7 to 211)   | 104 (73.2 to 149)   |  |  |
| B/Florida/4/2006 like strain (B; Day 21)      | 107 (82.4 to 139)   | 71.1 (56.5 to 89.7) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Summary of Geometric Mean Titers Ratios (GMTR) of influenza Vaccine Antibodies After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route

|                 |  |
|-----------------|--|
| End point title | Summary of Geometric Mean Titers Ratios (GMTR) of influenza Vaccine Antibodies After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route <sup>[2]</sup> |
|-----------------|--|

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique. Geometric mean titer ratio is the geometric mean of the individual post-vaccination/pre-vaccination titer of antibodies to the influenza virus antigens.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0 (pre-vaccination) and Day 21 post 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                         | 18 to 60 years      | 61 years or older   |  |  |
|--|---------------------|---------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 64                  | 65                  |  |  |
| Units: Titer ratios                      |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| A/Brisbane/59/2007 like strain (H1N1)    | 17.2 (11.9 to 24.9) | 4.8 (3.4 to 6.77)   |  |  |
| A/Brisbane/10/2007 like strain (H3N2)    | 13.3 (9.11 to 19.5) | 7.35 (5.23 to 10.3) |  |  |
| B/Florida/4/2006 like strain (B)         | 7.96 (5.65 to 11.2) | 3.06 (2.36 to 3.98) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects with Seroprotection Against the Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects with Seroprotection Against the Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route <sup>[3]</sup> |
|-----------------|--|

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique. Seroprotection was defined as titers  $\geq 40$  (1/dil) on Day 0 and Day 21.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|



End point timeframe:

Day 0 (pre-vaccination) and Day 21 post 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                              | 18 to 60 years  | 61 years or older |  |  |
|---|-----------------|-------------------|--|--|
| Subject group type                            | Reporting group | Reporting group   |  |  |
| Number of subjects analysed                   | 64              | 65                |  |  |
| Units: Percentage of subjects                 |                 |                   |  |  |
| number (not applicable)                       |                 |                   |  |  |
| A/Brisbane/59/2007 like strain (H1N1; Day 0)  | 28.1            | 40                |  |  |
| A/Brisbane/10/2007 like strain (H3N2; Day 0)  | 17.2            | 26.2              |  |  |
| B/Florida/4/2006 like strain (B; Day 0)       | 20.3            | 33.8              |  |  |
| A/Brisbane/59/2007 like strain (H1N1; Day 21) | 96.9            | 87.7              |  |  |
| A/Brisbane/10/2007 like strain (H3N2; Day 21) | 81.3            | 81.5              |  |  |
| B/Florida/4/2006 like strain (B; Day 21)      | 89.1            | 80                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Achieving Seroconversion or Significant Increase Against the Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by Intramuscular Route

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects Achieving Seroconversion or Significant Increase Against the Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by Intramuscular Route <sup>[4]</sup> |
|-----------------|---|

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique. Seroconversion was defined as subjects with a titer <10 (1/dil) on Day 0 and a post-injection titer ≥40 (1/dil) on Day 21 or significant increase was defined as subjects with a titer ≥10 (1/dil) on Day 0 and a ≥4-fold increase of post-injection titer on Day 21.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 21 post 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                      | 18 to 60 years  | 61 years or older |  |  |
|---------------------------------------|-----------------|-------------------|--|--|
| Subject group type                    | Reporting group | Reporting group   |  |  |
| Number of subjects analysed           | 64              | 65                |  |  |
| Units: Percentage of Subjects         |                 |                   |  |  |
| number (not applicable)               |                 |                   |  |  |
| A/Brisbane/59/2007 like strain (H1N1) | 79.7            | 47.7              |  |  |
| A/Brisbane/10/2007 like strain (H3N2) | 71.9            | 60                |  |  |
| B/Florida/4/2006 like strain (B)      | 64.1            | 27.7              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects with at Least One Reaction Corresponding to those Listed in the EMEA Note for Guidance Within 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation (Intramuscular Route)

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects with at Least One Reaction Corresponding to those Listed in the EMEA Note for Guidance Within 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation (Intramuscular Route) <sup>[5]</sup> |
|-----------------|--|

End point description:

Solicited injection site reactions: Induration and Ecchymosis. Solicited systemic reactions: Pyrexia, Malaise, and Shivering.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0 up to Day 3 post-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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                           | 18 to 60 years  | 61 years or older |  |  |
|--|-----------------|-------------------|--|--|
| Subject group type                         | Reporting group | Reporting group   |  |  |
| Number of subjects analysed                | 65              | 65                |  |  |
| Units: Percentage of subjects              |                 |                   |  |  |
| number (not applicable)                    |                 |                   |  |  |
| Injection site induration ≥5 cm for 4 days | 0               | 0                 |  |  |
| Injection site ecchymosis                  | 7.7             | 6.2               |  |  |
| Pyrexia (>38°C for at least 1 day)         | 1.5             | 0                 |  |  |
| Malaise                                    | 12.3            | 9.2               |  |  |
| Shivering                                  | 3.1             | 0                 |  |  |

## Statistical analyses

**Primary: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions within 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route**

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions within 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route <sup>[6]</sup> |
|-----------------|---|

End point description:

Solicited injection site: Pain, Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 injection site: Pain – Incapacitating, unable to perform usual activities; Erythema, Swelling, Induration, and Ecchymosis – ≥10 cm. Grade 3 systemic reactions: Fever – >39.0°C; Headache, Malaise, Myalgia, and Shivering – Prevents daily activity.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0 up to Day 3 post-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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                  | 18 to 60 years  | 61 years or older |  |  |
|-----------------------------------|-----------------|-------------------|--|--|
| Subject group type                | Reporting group | Reporting group   |  |  |
| Number of subjects analysed       | 65              | 65                |  |  |
| Units: Percentage of subjects     |                 |                   |  |  |
| number (not applicable)           |                 |                   |  |  |
| Injection site Pain               | 49.2            | 24.6              |  |  |
| Grade 3 Injection site Pain       | 0               | 0                 |  |  |
| Injection site Erythema           | 32.3            | 27.7              |  |  |
| Grade 3 Injection site Erythema   | 3.1             | 9.2               |  |  |
| Injection site Swelling           | 18.5            | 12.3              |  |  |
| Grade 3 Injection site Swelling   | 0               | 0                 |  |  |
| Injection site Induration         | 27.7            | 12.3              |  |  |
| Grade 3 Injection site Induration | 1.5             | 0                 |  |  |
| Injection site Ecchymosis         | 7.7             | 6.2               |  |  |
| Grade 3 Injection site Ecchymosis | 0               | 0                 |  |  |
| Fever                             | 10.8            | 4.6               |  |  |
| Grade 3 Fever                     | 0               | 0                 |  |  |
| Headache                          | 20              | 13.8              |  |  |
| Grade 3 Headache                  | 1.5             | 0                 |  |  |
| Malaise                           | 12.3            | 9.2               |  |  |
| Grade 3 Malaise                   | 0               | 0                 |  |  |
| Myalgia                           | 15.4            | 15.4              |  |  |
| Grade 3 Myalgia                   | 0               | 0                 |  |  |
| Shivering                         | 3.1             | 0                 |  |  |
| Grade 3 Shivering                 | 0               | 0                 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions More than 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects Reporting Solicited Injection-site or Systemic Reactions More than 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine, Northern Hemisphere 2008-2009 Formulation by the Intramuscular Route <sup>[7]</sup> |
|-----------------|--|

End point description:

Solicited injection site: Pain, Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 injection site: Pain – Incapacitating, unable to perform usual activities; Erythema, Swelling, Induration, and Ecchymosis – ≥10 cm. Grade 3 systemic reactions: Fever – >39.0°C; Headache, Malaise, Myalgia, and Shivering – Prevents daily activity.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

>Day 3 post-vaccination

Notes:

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

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values                  | 18 to 60 years  | 61 years or older |  |  |
|-----------------------------------|-----------------|-------------------|--|--|
| Subject group type                | Reporting group | Reporting group   |  |  |
| Number of subjects analysed       | 65              | 65                |  |  |
| Units: Percentage of subjects     |                 |                   |  |  |
| number (not applicable)           |                 |                   |  |  |
| Injection site Pain               | 49.2            | 24.6              |  |  |
| Grade 3 Injection site Pain       | 0               | 0                 |  |  |
| Injection site Erythema           | 32.3            | 27.7              |  |  |
| Grade 3 Injection site Erythema   | 3.1             | 9.2               |  |  |
| Injection site Swelling           | 18.5            | 12.3              |  |  |
| Grade 3 Injection site Swelling   | 0               | 0                 |  |  |
| Injection site Induration         | 27.7            | 12.3              |  |  |
| Grade 3 Injection site Induration | 1.5             | 0                 |  |  |
| Injection site Ecchymosis         | 7.7             | 6.2               |  |  |
| Grade 3 Injection site Ecchymosis | 0               | 0                 |  |  |
| Fever                             | 0               | 0                 |  |  |
| Grade 3 Fever                     | 0               | 0                 |  |  |
| Headache                          | 1.5             | 4.6               |  |  |
| Grade 3 Headache                  | 0               | 0                 |  |  |
| Malaise                           | 1.5             | 3.1               |  |  |
| Grade 3 Malaise                   | 0               | 0                 |  |  |
| Myalgia                           | 3.1             | 3.1               |  |  |
| Grade 3 Myalgia                   | 1.5             | 0                 |  |  |
| Shivering                         | 0               | 0                 |  |  |
| Grade 3 Shivering                 | 0               | 0                 |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 (post-vaccination) up to Day 21 post-vaccination.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 10.0 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | 18 to 60 years |
|-----------------------|----------------|

Reporting group description:

Subjects aged 18 to 60 years who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | 61 years or older |
|-----------------------|-------------------|

Reporting group description:

Subjects aged 61 years or older who received one dose of inactivated, split-virion influenza vaccine, Northern Hemisphere 2008-2009 formulation on day 0.

| Serious adverse events                            | 18 to 60 years | 61 years or older |  |
|---|----------------|-------------------|--|
| Total subjects affected by serious adverse events |                |                   |  |
| subjects affected / exposed                       | 0 / 65 (0.00%) | 0 / 65 (0.00%)    |  |
| number of deaths (all causes)                     | 0              | 0                 |  |
| number of deaths resulting from adverse events    | 0              | 0                 |  |

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

| Non-serious adverse events                            | 18 to 60 years   | 61 years or older |  |
|---|------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                  |                   |  |
| subjects affected / exposed                           | 32 / 65 (49.23%) | 18 / 65 (27.69%)  |  |
| Nervous system disorders                              |                  |                   |  |
| Headache  |                  |                   |  |
| alternative assessment type: Systematic               |                  |                   |  |
| subjects affected / exposed                           | 13 / 65 (20.00%) | 9 / 65 (13.85%)   |  |
| occurrences (all)                                     | 13               | 9                 |  |
| General disorders and administration site conditions  |                  |                   |  |
| Injection site ecchymosis                             |                  |                   |  |
| alternative assessment type: Systematic               |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 65 (7.69%)   | 4 / 65 (6.15%)   |  |
| occurrences (all)                               | 5                | 4                |  |
| Malaise   |                  |                  |  |
| alternative assessment type:<br>Systematic      |                  |                  |  |
| subjects affected / exposed                     | 8 / 65 (12.31%)  | 6 / 65 (9.23%)   |  |
| occurrences (all)                               | 8                | 6                |  |
| Injection site pain                             |                  |                  |  |
| alternative assessment type:<br>Systematic      |                  |                  |  |
| subjects affected / exposed                     | 32 / 65 (49.23%) | 16 / 65 (24.62%) |  |
| occurrences (all)                               | 32               | 16               |  |
| Injection site erythema                         |                  |                  |  |
| alternative assessment type:<br>Systematic      |                  |                  |  |
| subjects affected / exposed                     | 21 / 65 (32.31%) | 18 / 65 (27.69%) |  |
| occurrences (all)                               | 21               | 18               |  |
| Injection site swelling                         |                  |                  |  |
| alternative assessment type:<br>Systematic      |                  |                  |  |
| subjects affected / exposed                     | 12 / 65 (18.46%) | 8 / 65 (12.31%)  |  |
| occurrences (all)                               | 12               | 8                |  |
| Injection site induration                       |                  |                  |  |
| alternative assessment type:<br>Systematic      |                  |                  |  |
| subjects affected / exposed                     | 18 / 65 (27.69%) | 8 / 65 (12.31%)  |  |
| occurrences (all)                               | 18               | 8                |  |
| Fever   |                  |                  |  |
| alternative assessment type:<br>Systematic      |                  |                  |  |
| subjects affected / exposed                     | 7 / 65 (10.77%)  | 3 / 65 (4.62%)   |  |
| occurrences (all)                               | 7                | 3                |  |
| Musculoskeletal and connective tissue disorders |                  |                  |  |
| Myalgia   |                  |                  |  |
| alternative assessment type:<br>Systematic      |                  |                  |  |
| subjects affected / exposed                     | 10 / 65 (15.38%) | 10 / 65 (15.38%) |  |
| occurrences (all)                               | 10               | 10               |  |

## **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**

None reported