# Clinical trial results:
# Evaluation of the Cellular, Humoral and Mucosal Immune Response in Adults and Elderly Subjects Vaccinated either with an Inactivated Influenza Vaccine Administered via the Intradermal Route or an Inactivated Influenza Vaccine Administered via the Intramuscular Route

## Summary

| | |
|---|---|
| EudraCT number | 2007-002104-18 |
| Trial protocol | FR |
| Global end of trial date | 05 May 2008 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 16 February 2016 |
| First version publication date | 01 April 2015 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | GID25 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00776438 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Sanofi Pasteur SA |
| Sponsor organisation address | 2, avenue Pont Pasteur, F-69367 Lyon Cedex 07, France, |
| Public contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (4) 37 37 58 50, stephanie.pepin@sanofipasteur.com |
| Scientific contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (4) 37 37 58 50, stephanie.pepin@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:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 19 February 2009 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 05 May 2008 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

- To describe the cellular immune response per age group (adults or elderly) and vaccine group (Intradermal [ID] influenza or Intramuscular [IM] comparator vaccines) before vaccination and 7 days, 10 days, 14 days, 21 days, and 180 days after vaccination
- To describe the humoral immune response per age group and vaccine group before vaccination, 14 days, 21 days, and 180 days after vaccination
- To describe mucosal immunity per age group and vaccine group through quantification of influenza-specific IgA (total, specific and sub-classes: IgA1 and IgA2) collected from saliva and serum before vaccination and 10 days, 14 days, 21 days and 180 days after vaccination
- To describe the safety of the vaccines per age group and per vaccine group after vaccination

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and 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.

Background therapy:

Not applicable

Evidence for comparator:

As recommended by the WHO, the influenza vaccine (split-virion, inactivated) Vaxigrip® 2007-2008 NH formulation was used as the control product and administered by the IM route.

| | |
|---|---|
| Actual start date of recruitment | 17 September 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 | France: 160 |
| Worldwide total number of subjects | 160 |
| EEA total number of subjects | 160 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 119 |
| From 65 to 84 years | 41 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Study subjects were enrolled from 17 September 2007 to 09 November 2007 at 1 clinical center in France.

### Pre-assignment

Screening details:

A total of 160 subjects who met all the 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 | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

Not applicable

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Adult - ID 9µg |

Arm description:

Adults 18-40 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (9 µg).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Intradermal Influenza Vaccine |
| Investigational medicinal product code | 333 |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intradermal use |

Dosage and administration details:

0.1 mL dose (9 µg strength), intradermal use into the upper arm (deltoid area), one dose on V01.

| | |
|---|---|
| **Arm title** | Adult - IM 15µg |

Arm description:

Adults 18-40 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg).

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Vaxigrip® |
| Investigational medicinal product code | |
| Other name | Inactivated, split-virion, influenza virus (H3N2 strain) |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL dose (15 µg strength), intramuscular use into the upper arm (deltoid area), one dose on Day 0.

| | |
|---|---|
| **Arm title** | Elderly - ID 15µg |

Arm description:

Elderly subjects 60-85 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (15 µg).

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Intradermal Influenza Vaccine |
| Investigational medicinal product code | 333 |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intradermal use |

Dosage and administration details:

0.1 mL dose (15 µg strength), intradermal use into the upper arm (deltoid area), one dose on Day 0.

| **Arm title** | Elderly - IM 15µg |
|---|---|

Arm description:

Elderly subjects 60-85 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg).

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Vaxigrip® |
| Investigational medicinal product code | |
| Other name | Inactivated, split-virion, influenza virus (H3N2 strain) |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL dose (15 µg strength), intramuscular use into the upper arm (deltoid area), one dose on Day 0.

| **Number of subjects in period 1** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg |
|---|---|---|---|
| Started | 38 | 42 | 40 |
| Completed | 35 | 41 | 39 |
| Not completed | 3 | 1 | 1 |
| Consent withdrawn by subject | 1 | 1 | 1 |
| Lost to follow-up | 1 | - | - |
| Protocol deviation | 1 | - | - |

| **Number of subjects in period 1** | Elderly - IM 15µg |
|---|---|
| Started | 40 |
| Completed | 40 |
| Not completed | 0 |
| Consent withdrawn by subject | - |
| Lost to follow-up | - |
| Protocol deviation | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Adult - ID 9µg |
| Reporting group description: | |
| Adults 18-40 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (9 µg). | |
| Reporting group title | Adult - IM 15µg |
| Reporting group description: | |
| Adults 18-40 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg). | |
| Reporting group title | Elderly - ID 15µg |
| Reporting group description: | |
| Elderly subjects 60-85 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (15 µg). | |
| Reporting group title | Elderly - IM 15µg |
| Reporting group description: | |
| Elderly subjects 60-85 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg). | |

| Reporting group values | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg |
|---|---|---|---|
| Number of subjects | 38 | 42 | 40 |
| Age categorical<br>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) | 38 | 42 | 19 |
| From 65-84 years | 0 | 0 | 21 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 26.6 | 25.7 | 65.7 |
| standard deviation | ± 5.7 | ± 4.8 | ± 5 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 26 | 30 | 17 |
| Male | 12 | 12 | 23 |

| Reporting group values | Elderly - IM 15µg | Total | |
|---|---|---|---|
| Number of subjects | 40 | 160 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 20 | 119 | |
| From 65-84 years | 20 | 41 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 65.9 | | |
| standard deviation | ± 4 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 22 | 95 | |
| Male | 18 | 65 | |

## End points

### End points reporting groups

| Reporting group title | Adult - ID 9µg |
|---|---|
| Reporting group description: | |
| Adults 18-40 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (9 µg). | |
| Reporting group title | Adult - IM 15µg |
| Reporting group description: | |
| Adults 18-40 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg). | |
| Reporting group title | Elderly - ID 15µg |
| Reporting group description: | |
| Elderly subjects 60-85 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (15 µg). | |
| Reporting group title | Elderly - IM 15µg |
| Reporting group description: | |
| Elderly subjects 60-85 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg). | |

### Primary: Median Percentage of IFN-γ and TNF-α Single Secreting CD4 T Cells Specific for each of the Influenza Vaccine Strains Before Vaccination in Adults and Elderly Subjects Randomized to Either Intradermal or Intramuscular Route

| End point title | Median Percentage of IFN-γ and TNF-α Single Secreting CD4 T Cells Specific for each of the Influenza Vaccine Strains Before Vaccination in Adults and Elderly Subjects Randomized to Either Intradermal or Intramuscular Route[1] |
|---|---|
| End point description: | |
| Cellular immune response was assessed using the intracellular cytokine staining (ICS) method. | |
| End point type | Primary |
| End point timeframe: | |
| Day 0 (pre-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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Median percentage of CD4 T cells | | | | |
| number (not applicable) | | | | |
| A/H1N1 Solomon Island; IFN-γ+ | 0.135 | 0.1 | 0.05 | 0.05 |
| A/H3N2 Wisconsin; IFN-γ+ | 0.315 | 0.34 | 0.185 | 0.13 |
| B/Malaysia; IFN-γ+ | 0.51 | 0.5 | 0.17 | 0.16 |
| A/H1N1 Solomon Island; TNF-α+ | 0.18 | 0.14 | 0.14 | 0.07 |
| A/H3N2 Wisconsin; TNF-α+ | 0.114 | 0.155 | 0.095 | 0.06 |
| B/Malaysia; TNF-α+ | 0.2 | 0.18 | 0.14 | 0.13 |
| A/H1N1 Solomon Island; IL-2+ | 0.06 | 0.05 | 0.05 | 0.02 |
| A/H3N2 Wisconsin; IL-2+ | 0.03 | 0.02 | 0.02 | 0.01 |

| | | | | |
|---|---|---|---|---|
| B/Malaysia; IL-2+ | 0.085 | 0.06 | 0.07 | 0.03 |
| A/H1N1 Solomon Island; IFN-γ+/IL-2+ | 0.035 | 0.027 | 0.015 | 0.007 |
| A/H3N2 Wisconsin; IFN-γ+/IL-2+ | 0.015 | 0.01 | 0.01 | 0.005 |
| B/Malaysia; IFN-γ+/IL-2+ | 0.045 | 0.035 | 0.025 | 0.02 |
| A/H1N1 Solomon Island; TNF-α+/IL-2+ | 0.035 | 0.03 | 0.027 | 0.02 |
| A/H3N2 Wisconsin; TNF-α+/IL-2+ | 0.012 | 0.01 | 0.01 | 0.01 |
| B/Malaysia; TNF-α+/IL-2+ | 0.05 | 0.042 | 0.04 | 0.025 |
| A/H1N1 Solomon Island; IFN-γ+/TNF-α+ | 0.04 | 0.032 | 0.015 | 0.012 |
| A/H3N2 Wisconsin; IFN-γ+/TNF-α+ | 0.035 | 0.035 | 0.015 | 0.007 |
| B/Malaysia; IFN-γ+/TNF-α+ | 0.075 | 0.055 | 0.03 | 0.03 |
| A/H1N1 Solomon Island; IFN-γ+/TNF-α+/IL-2+ | 0.025 | 0.022 | 0.012 | 0.005 |
| A/H3N2 Wisconsin; IFN-γ+/TNF-α+/IL-2+ | 0.005 | 0.005 | 0.005 | 0.005 |
| B/Malaysia; IFN-γ+/TNF-α+/IL-2+ | 0.035 | 0.025 | 0.015 | 0.012 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Ratios of Cytokine Secreting CD8 T Cell in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Either Intradermal or Intramuscular Route

| | |
|---|---|
| End point title | Geometric Mean Ratios of Cytokine Secreting CD8 T Cell in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Either Intradermal or Intramuscular Route[2] |

End point description:

Cellular immune response was assessed using the intracellular cytokine staining (ICS) method.

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

End point timeframe:

Day 0 (pre-vaccination) and Day 7, 10, 14, 21, and 180 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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| IFN-γ+; A/H1N1 Solomon Island (D7/D0) | 0.771 (0.614 to 0.967) | 1.04 (0.772 to 1.39) | 1.22 (0.885 to 1.68) | 1.57 (0.958 to 2.58) |
| IFN-γ+; A/H3N2 Wisconsin (D7/D0) | 0.722 (0.555 to 0.939) | 0.842 (0.621 to 1.14) | 0.737 (0.469 to 1.16) | 1.24 (0.873 to 1.76) |
| IFN-γ+; B/Malaysia (D7/D0) | 0.974 (0.763 to 1.24) | 1.04 (0.749 to 1.46) | 1.1 (0.877 to 1.38) | 1.55 (0.766 to 3.14) |
| IFN-γ+; A/H1N1 Solomon Island (D10/D0) | 0.906 (0.705 to 1.16) | 0.843 (0.615 to 1.16) | 1.13 (0.816 to 1.57) | 1.11 (0.73 to 1.69) |

| | | | | |
|---|---|---|---|---|
| IFN-γ+; A/H3N2 Wisconsin (D10/D0) | 0.736 (0.541 to 1) | 0.893 (0.673 to 1.18) | 0.818 (0.642 to 1.04) | 1.18 (0.875 to 1.59) |
| IFN-γ+; B/Malaysia (D10/D0) | 0.948 (0.682 to 1.32) | 1.18 (0.879 to 1.59) | 0.875 (0.603 to 1.27) | 1.33 (0.859 to 2.07) |
| IFN-γ+; A/H1N1 Solomon Island (D14/D0) | 0.969 (0.714 to 1.31) | 1.15 (0.881 to 1.5) | 1.16 (0.872 to 1.54) | 1.23 (0.867 to 1.75) |
| IFN-γ+; A/H3N2 Wisconsin (D14/D0) | 0.82 (0.635 to 1.06) | 0.968 (0.724 to 1.29) | 0.72 (0.489 to 1.06) | 1.23 (0.927 to 1.64) |
| IFN-γ+; B/Malaysia (D14/D0) | 0.956 (0.702 to 1.3) | 1.24 (0.918 to 1.68) | 0.691 (0.463 to 1.03) | 1.11 (0.68 to 1.8) |
| IFN-γ+; A/H1N1 Solomon Island (D21/D0) | 0.916 (0.737 to 1.14) | 1.05 (0.746 to 1.47) | 0.977 (0.76 to 1.26) | 1.2 (0.721 to 1.98) |
| IFN-γ+; A/H3N2 Wisconsin (D21/D0) | 0.949 (0.806 to 1) | 0.99 (0.739 to 1.33) | 1.13 (0.874 to 1.45) | 1.14 (0.783 to 1.67) |
| IFN-γ+; B/Malaysia (D21/D0) | 1.01 (0.763 to 1.34) | 1.24 (0.921 to 1.66) | 1.11 (0.711 to 1.73) | 1.12 (0.639 to 1.95) |
| IFN-γ+; A/H1N1 Solomon Island (D180/D0) | 0.963 (0.608 to 1.53) | 1.13 (0.791 to 1.62) | 0.913 (0.503 to 1.66) | 1.47 (0.919 to 2.35) |
| IFN-γ+; A/H3N2 Wisconsin (D180/D0) | 1.48 (1.12 to 1.95) | 1.28 (0.89 to 1.83) | 0.998 (0.644 to 1.55) | 2 (1.47 to 2.74) |
| IFN-γ+; B/Malaysia (D180/D0) | 1.19 (0.847 to 1.67) | 1.28 (0.909 to 1.8) | 1.03 (0.722 to 1.46) | 1.94 (1.01 to 3.7) |
| TNF-α+; A/H1N1 Solomon Island (D7/D0) | 0.869 (0.664 to 1.14) | 1.01 (0.753 to 1.35) | 1.2 (0.866 to 1.68) | 1.66 (0.821 to 3.35) |
| TNF-α+; A/H3N2 Wisconsin (D7/D0) | 1.02 (0.666 to 1.55) | 1.03 (0.633 to 1.66) | 1.09 (0.57 to 2.09) | 1.36 (0.717 to 2.57) |
| TNF-α+; B/Malaysia (D7/D0) | 1.08 (0.702 to 1.67) | 1.01 (0.68 to 1.5) | 0.84 (0.483 to 1.46) | 1.21 (0.627 to 2.35) |
| TNF-α+; A/H1N1 Solomon Island (D10/D0) | 1.07 (0.83 to 1.37) | 0.835 (0.616 to 1.13) | 0.917 (0.725 to 1.16) | 0.972 (0.598 to 1.58) |
| TNF-α+; A/H3N2 Wisconsin (D10/D0) | 0.82 (0.49 to 1.37) | 1.08 (0.714 to 1.63) | 1.19 (0.83 to 1.72) | 1.1 (0.635 to 1.9) |
| TNF-α+; B/Malaysia (D10/D0) | 0.948 (0.58 to 1.55) | 1.26 (0.879 to 1.79) | 1.15 (0.735 to 1.8) | 1.05 (0.776 to 1.43) |
| TNF-α+; A/H1N1 Solomon Island (D14/D0) | 0.869 (0.591 to 1.28) | 1.09 (0.858 to 1.38) | 1.24 (0.685 to 2.24) | 1.49 (0.935 to 2.37) |
| TNF-α+; A/H3N2 Wisconsin (D14/D0) | 0.908 (0.557 to 1.48) | 1.12 (0.816 to 1.55) | 0.972 (0.536 to 1.76) | 1.01 (0.583 to 1.76) |
| TNF-α+; B/Malaysia (D14/D0) | 1 (0.63 to 1.6) | 1.3 (0.913 to 1.86) | 0.86 (0.566 to 1.31) | 1.06 (0.786 to 1.43) |
| TNF-α+; A/H1N1 Solomon Island (D21/D0) | 0.953 (0.708 to 1.28) | 0.972 (0.747 to 1.27) | 1.01 (0.716 to 1.44) | 0.843 (0.522 to 1.36) |
| TNF-α+; A/H3N2 Wisconsin (D21/D0) | 1.04 (0.622 to 1.74) | 0.902 (0.584 to 1.39) | 0.983 (0.601 to 1.61) | 1.13 (0.647 to 1.98) |
| TNF-α+; B/Malaysia (D21/D0) | 1.03 (0.648 to 1.64) | 1.17 (0.761 to 1.8) | 1.21 (0.69 to 2.13) | 1.28 (0.853 to 1.92) |
| TNF-α+; A/H1N1 Solomon Island (D180/D0) | 0.774 (0.466 to 1.29) | 1.09 (0.792 to 1.5) | 1.2 (0.688 to 2.09) | 1.26 (0.805 to 1.98) |
| TNF-α+; A/H3N2 Wisconsin (D180/D0) | 1.21 (0.627 to 2.34) | 1.23 (0.732 to 2.07) | 1.04 (0.599 to 1.79) | 1.19 (0.673 to 2.1) |
| TNF-α+; B/Malaysia (D180/D0) | 0.944 (0.521 to 1.71) | 1.23 (0.767 to 1.97) | 1.13 (0.722 to 1.76) | 1.71 (1.03 to 2.85) |
| IL-2+; A/H1N1 Solomon Island (D7/D0) | 0.809 (0.648 to 1.01) | 0.803 (0.583 to 1.11) | 1.31 (0.957 to 1.78) | 1.28 (0.763 to 2.15) |
| IL-2+; A/H3N2 Wisconsin (D7/D0) | 0.9 (0.633 to 1.28) | 1.1 (0.694 to 1.75) | 1.17 (0.627 to 2.2) | 1.41 (0.754 to 2.62) |
| IL-2+; B/Malaysia (D7/D0) | 0.705 (0.542 to 0.918) | 1.12 (0.802 to 1.55) | 0.824 (0.545 to 1.24) | 0.803 (0.552 to 1.17) |
| IL-2+; A/H1N1 Solomon Island (D10/D0) | 0.706 (0.487 to 1.02) | 0.973 (0.704 to 1.35) | 1.11 (0.809 to 1.54) | 1.07 (0.584 to 1.94) |
| IL-2+; A/H3N2 Wisconsin (D10/D0) | 0.733 (0.478 to 1.13) | 1.23 (0.854 to 1.78) | 0.731 (0.479 to 1.12) | 0.987 (0.592 to 1.64) |

| | | | | |
|---|---|---|---|---|
| IL-2+; B/Malaysia (D10/D0) | 0.648 (0.435 to 0.965) | 1.22 (0.815 to 1.82) | 1.02 (0.657 to 1.58) | 0.881 (0.6 to 1.29) |
| IL-2+; A/H1N1 Solomon Island (D14/D0) | 0.811 (0.575 to 1.14) | 1.12 (0.774 to 1.63) | 1.02 (0.709 to 1.47) | 1.66 (1.06 to 2.62) |
| IL-2+; A/H3N2 Wisconsin (D14/D0) | 0.757 (0.521 to 1.1) | 1.03 (0.637 to 1.66) | 0.816 (0.428 to 1.55) | 1.45 (0.943 to 2.22) |
| IL-2+; B/Malaysia (D14/D0) | 0.638 (0.393 to 1.04) | 1.43 (0.99 to 2.06) | 0.936 (0.637 to 1.37) | 0.993 (0.756 to 1.3) |
| IL-2+; A/H1N1 Solomon Island (D21/D0) | 0.819 (0.614 to 1.09) | 0.93 (0.619 to 1.4) | 0.815 (0.508 to 1.31) | 1.17 (0.768 to 1.79) |
| IL-2+; A/H3N2 Wisconsin (D21/D0) | 0.837 (0.528 to 1.33) | 1.04 (0.597 to 1.81) | 0.764 (0.529 to 1.1) | 1.4 (0.812 to 2.41) |
| IL-2+; B/Malaysia (D21/D0) | 0.808 (0.589 to 1.11) | 1.31 (0.812 to 2.1) | 0.634 (0.319 to 1.26) | 1.29 (0.911 to 1.83) |
| IL-2+; A/H1N1 Solomon Island (D180/D0) | 0.741 (0.512 to 1.07) | 1.2 (0.809 to 1.79) | 1.05 (0.69 to 1.61) | 1.81 (1.22 to 2.68) |
| IL-2+; A/H3N2 Wisconsin (D180/D0) | 0.801 (0.418 to 1.53) | 1.76 (0.958 to 3.24) | 0.512 (0.198 to 1.32) | 2.14 (1.2 to 3.81) |
| IL-2+; B/Malaysia (D180/D0) | 0.671 (0.455 to 0.988) | 1.65 (1.01 to 2.68) | 0.945 (0.558 to 1.6) | 1.77 (1.17 to 2.68) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Summary of Anti-HA Lymphoproliferative Response in terms of Geometric Mean of Counts per minute and Stimulation Index in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| | |
|---|---|
| End point title | Summary of Anti-HA Lymphoproliferative Response in terms of Geometric Mean of Counts per minute and Stimulation Index in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[3] |

End point description:

Corrected lymphoproliferation (cpm) and stimulation index (SI) were assessed using the lymphoproliferation method with H1N1/Solomon Island rHA protein.

| | |
|---|---|
| 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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Counts per minute and Stimulation index | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Corrected lymphoproliferation (cpm); D0 | 9433 (6569 to 13545) | 10250 (7836 to 13408) | 6171 (4635 to 8217) | 4603 (3639 to 5822) |

| | | | | |
|---|---|---|---|---|
| Stimulation index (SI); D0 | 5.81 (4.5 to 7.5) | 4.3 (3.48 to 5.33) | 3.66 (3.06 to 4.38) | 3.11 (2.67 to 3.62) |
| Corrected lymphoproliferation (cpm); D21 | 12822 (8576 to 19170) | 17070 (13582 to 21452) | 10402 (7347 to 14729) | 8816 (6171 to 12595) |
| Stimulation index (SI); D21 | 6.52 (4.92 to 8.63) | 5.92 (4.76 to 7.36) | 5.17 (4.21 to 6.35) | 4.79 (3.73 to 6.15) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects with Stimulation index (SI) Titers ≥3 and corrected lymphoproliferation ≥3000 Counts per minute in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| | |
|---|---|
| End point title | Percentage of Subjects with Stimulation index (SI) Titers ≥3 and corrected lymphoproliferation ≥3000 Counts per minute in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[4] |

End point description:

Stimulation index (SI) ≥3 and corrected lymphoproliferation (cpm) were assessed using the lymphoproliferation method with H1N1/Solomon Island rHA protein.

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

End point timeframe:

Day 0 (pre-vaccination) and 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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| SI ≥3, corrected lymphoproliferation;D0;≥3000 cpm | 76.7 | 63.2 | 55.6 | 41.7 |
| SI ≥3, corrected lymphoproliferation;D21;≥3000 cpm | 75.9 | 86.8 | 82.9 | 69.4 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers of HI Antibody Response to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| | |
|---|---|
| End point title | Geometric Mean Titers of HI Antibody Response to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with |

| | |
|---|---|
| | an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[5] |

End point description:

The humoral immune response was assessed using the hemagglutination inhibition (HI) test.

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

End point timeframe:

Day 0 (pre-vaccination) and Day 14, 21, and 180 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** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titer (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/Solomon Island/3/2006 (H1N1); D0 | 31.8 (16.5 to 61.6) | 48 (27.1 to 85) | 10.3 (7.18 to 14.7) | 8.41 (6.53 to 10.8) |
| A/Solomon Island/3/2006 (H1N1); D14 | 840 (487 to 1449) | 742 (491 to 1123) | 232 (155 to 349) | 143 (86.5 to 236) |
| A/Solomon Island/3/2006 (H1N1); D21 | 622 (373 to 1037) | 580 (377 to 892) | 230 (152 to 350) | 148 (90.5 to 242) |
| A/Solomon Island/3/2006 (H1N1); D180 | 245 (159 to 377) | 219 (150 to 320) | 65.8 (45.8 to 94.5) | 46.3 (28.8 to 74.5) |
| A/Wisconsin/67/2005 (H3N2); D0 | 59.2 (34.8 to 101) | 54.7 (33.2 to 90.1) | 33.3 (18.1 to 61.5) | 29.5 (18.1 to 48.3) |
| A/Wisconsin/67/2005 (H3N2); D14 | 516 (365 to 728) | 496 (356 to 690) | 634 (420 to 957) | 469 (308 to 713) |
| A/Wisconsin/67/2005 (H3N2); D21 | 488 (341 to 699) | 468 (326 to 671) | 663 (444 to 991) | 511 (336 to 778) |
| A/Wisconsin/67/2005 (H3N2); D180 | 215 (144 to 321) | 183 (132 to 255) | 159 (106 to 236) | 139 (96.7 to 201) |
| B/Malaysia/2506/2004; D0 | 12.9 (9.01 to 18.5) | 18.7 (13.1 to 26.7) | 10.9 (8.41 to 14.1) | 8.56 (6.57 to 11.1) |
| B/Malaysia/2506/2004; D14 | 91.2 (64.6 to 129) | 181 (129 to 255) | 75.8 (47.6 to 121) | 41.8 (26.8 to 65.1) |
| B/Malaysia/2506/2004; D21 | 78.5 (54.5 to 113) | 156 (114 to 214) | 74.5 (46.6 to 119) | 38.6 (25.4 to 58.9) |
| B/Malaysia/2506/2004; D180 | 22.3 (14.8 to 33.6) | 39.7 (28.7 to 54.8) | 16.3 (11 to 24.2) | 12.9 (9.42 to 17.6) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers Ratios of HI Antibody Response to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| End point title | Geometric Mean Titers Ratios of HI Antibody Response to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[6] |
|---|---|

End point description:

The humoral immune response was assessed using the hemagglutination inhibition (HI) test.

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

End point timeframe:

Day 0 (pre-vaccination) and Day 14, 21, and 180 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** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/Solomon Island/3/2006 (H1N1); D14/D0 | 25.1 (11.5 to 54.9) | 15.5 (7.86 to 30.5) | 22.2 (14.6 to 33.9) | 17 (10.6 to 27.2) |
| A/Solomon Island/3/2006 (H1N1); D21/D0 | 18.6 (8.87 to 39) | 12.1 (6.16 to 23.7) | 22 (14.8 to 32.7) | 17.6 (11 to 28.2) |
| A/Solomon Island/3/2006 (H1N1); D180/D0 | 7.61 (3.98 to 14.6) | 4.39 (2.41 to 8.01) | 6.7 (4.52 to 9.92) | 5.51 (3.47 to 8.75) |
| A/Wisconsin/67/2005 (H3N2); D14/D0 | 8.7 (4.88 to 15.5) | 9.05 (5.28 to 15.5) | 18.8 (9.21 to 38.3) | 15.9 (8.36 to 30.1) |
| A/Wisconsin/67/2005 (H3N2); D21/D0 | 8.23 (4.85 to 14) | 8.55 (4.71 to 15.5) | 19.6 (9.74 to 39.6) | 17.3 (9.6 to 31.2) |
| A/Wisconsin/67/2005 (H3N2); D180/D0 | 3.84 (2.36 to 6.26) | 3.16 (1.95 to 5.12) | 5 (2.77 to 9) | 4.72 (2.84 to 7.84) |
| B/Malaysia/2506/2004; D14/D0 | 7.28 (4.77 to 11.1) | 9.67 (5.6 to 16.7) | 6.82 (4.29 to 10.8) | 4.88 (3.32 to 7.17) |
| B/Malaysia/2506/2004; D21/D0 | 6.27 (4.11 to 9.58) | 8.34 (5 to 13.9) | 6.7 (4.26 to 10.5) | 4.52 (3.22 to 6.33) |
| B/Malaysia/2506/2004; D180/D0 | 1.79 (1.19 to 2.7) | 2.14 (1.37 to 3.34) | 1.56 (1.08 to 2.25) | 1.5 (1.25 to 1.81) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects with HI Antibody Titers ≥10 (1/dil) and ≥40 (1/dil) of HI Antibody Response to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine, Intradermal or Intramuscular Route

| End point title | Percentage of Subjects with HI Antibody Titers ≥10 (1/dil) and ≥40 (1/dil) of HI Antibody Response to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine, Intradermal or Intramuscular Route[7] |
|---|---|

End point description:

The humoral immune response was assessed using the hemagglutination inhibition (HI) test.

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

End point timeframe:

Day 0 (pre-vaccination) and Day 14, 21, and 180 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** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| A/Solomon Island/3/2006 (H1N1); ≥10 (1/dil); D0 | 65.8 | 76.2 | 35 | 30 |
| A/Solomon Island/3/2006 (H1N1); ≥10 (1/dil); D14 | 97.3 | 100 | 100 | 97.5 |
| A/Solomon Island/3/2006 (H1N1); ≥10 (1/dil); D21 | 100 | 100 | 100 | 97.5 |
| A/Solomon Island/3/2006 (H1N1); ≥10 (1/dil); D180 | 100 | 100 | 100 | 87.5 |
| A/Wisconsin/67/2005 (H3N2); ≥10 (1/dil); D0 | 89.5 | 81 | 60 | 70 |
| A/Wisconsin/67/2005 (H3N2); ≥10 (1/dil); D14 | 100 | 100 | 100 | 100 |
| A/Wisconsin/67/2005 (H3N2); ≥10 (1/dil); D21 | 100 | 100 | 100 | 100 |
| A/Wisconsin/67/2005 (H3N2); ≥10 (1/dil); D180 | 100 | 100 | 97.4 | 100 |
| B/Malaysia/2506/2004; ≥10 (1/dil); D0 | 52.6 | 71.4 | 60 | 32.5 |
| B/Malaysia/2506/2004; ≥10 (1/dil); D14 | 100 | 100 | 97.4 | 90 |
| B/Malaysia/2506/2004; ≥10 (1/dil); D21 | 97.3 | 100 | 94.9 | 87.5 |
| B/Malaysia/2506/2004; ≥10 (1/dil); D180 | 77.1 | 90.2 | 53.8 | 52.5 |
| A/Solomon Island/3/2006 (H1N1); ≥40 (1/dil); D0 | 36.8 | 50 | 15 | 5 |
| A/Solomon Island/3/2006 (H1N1); ≥40 (1/dil); D14 | 97.3 | 97.6 | 94.9 | 72.5 |
| A/Solomon Island/3/2006 (H1N1); ≥40 (1/dil); D21 | 94.6 | 97.6 | 92.3 | 77.5 |
| A/Solomon Island/3/2006 (H1N1); ≥40 (1/dil); D180 | 94.3 | 90.2 | 71.8 | 55 |
| A/Wisconsin/67/2005 (H3N2); ≥40 (1/dil); D0 | 57.9 | 61.9 | 42.5 | 45 |
| A/Wisconsin/67/2005 (H3N2); ≥40 (1/dil); D14 | 100 | 97.6 | 97.4 | 97.5 |
| A/Wisconsin/67/2005 (H3N2); ≥40 (1/dil); D21 | 100 | 97.6 | 100 | 97.5 |
| A/Wisconsin/67/2005 (H3N2); ≥40 (1/dil); D180 | 94.3 | 92.7 | 92.3 | 87.5 |
| B/Malaysia/2506/2004; ≥40 (1/dil); D0 | 15.8 | 31 | 10 | 7.5 |
| B/Malaysia/2506/2004; ≥40 (1/dil); D14 | 75.7 | 95.2 | 69.2 | 55 |
| B/Malaysia/2506/2004; ≥40 (1/dil); D21 | 75.7 | 95.2 | 69.2 | 57.5 |
| B/Malaysia/2506/2004; ≥40 (1/dil); D180 | 37.1 | 56.1 | 25.6 | 17.5 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Achieving Seroconversion or significant increase in HI Antibody Titers to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine, Intradermal or Intramuscular Route

| End point title | Percentage of Subjects Achieving Seroconversion or significant increase in HI Antibody Titers to the Three Influenza Strains in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine, Intradermal or Intramuscular Route[8] |
|---|---|

End point description:

The humoral immune response was assessed using the hemagglutination inhibition (HI) test. Seroconversion was defined as subjects with pre-vaccination titer <10 (1/dil) and with a post-vaccination titer ≥40 (1/dil) or significant increase was subjects with pre-vaccination titer ≥10 (1/dil) and with at least a 4-fold increase in post-vaccination titer.

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

End point timeframe:

Day 14, 21, and 180 post-vaccination

Notes:

[8] - 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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| A/Solomon Island/3/2006 (H1N1); % from D0 to D14 | 67.6 | 69 | 89.7 | 70 |
| A/Solomon Island/3/2006 (H1N1); % from D0 to D21 | 64.9 | 64.3 | 89.7 | 75 |
| A/Solomon Island/3/2006 (H1N1); % from D0 to D180 | 62.9 | 53.7 | 61.5 | 47.5 |
| A/Wisconsin/67/2005 (H3N2); % from D0 to D14 | 64.9 | 61.9 | 74.4 | 70 |
| A/Wisconsin/67/2005 (H3N2); % from D0 to D21 | 64.9 | 59.5 | 74.4 | 77.5 |
| A/Wisconsin/67/2005 (H3N2); % from D0 to D180 | 48.6 | 36.6 | 53.8 | 47.5 |
| B/Malaysia/2506/2004; % from D0 to D14 | 62.2 | 61.9 | 53.8 | 47.5 |
| B/Malaysia/2506/2004; % from D0 to D21 | 62.2 | 59.5 | 59 | 50 |
| B/Malaysia/2506/2004; % from D0 to D180 | 22.9 | 31.7 | 23.1 | 10 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers of Total IgA in Saliva of Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| End point title | Geometric Mean Titers of Total IgA in Saliva of Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[9] |
|---|---|

End point description:

Total IgA in saliva was assessed using enzyme-linked immunosorbent assay (ELISA).

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

End point timeframe:

Day 0 (pre-vaccination) and Day 10, 14, 21, and 180 post-vaccination

Notes:

[9] - 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** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titer (ng/ml) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| D0 | 130608 (93649 to 182154) | 81778 (50699 to 131907) | 115442 (76865 to 173380) | 99384 (63881 to 154619) |
| D10 | 124903 (79607 to 195973) | 114031 (69895 to 186036) | 97388 (66194 to 143282) | 70962 (34575 to 145642) |
| D14 | 113865 (75974 to 170652) | 99307 (54808 to 179933) | 100716 (68675 to 147706) | 76240 (48323 to 120286) |
| D21 | 125350 (85475 to 183828) | 68756 (31519 to 149984) | 103559 (66312 to 161727) | 75544 (45150 to 126398) |
| D180 | 111895 (55914 to 223926) | 74631 (32184 to 173062) | 67597 (29170 to 156645) | 39339 (14098 to 109768) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers Ratios of Total IgA in Saliva in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| End point title | Geometric Mean Titers Ratios of Total IgA in Saliva in Adults |
|---|---|

| | |
|---|---|
| | and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[10] |

End point description:

Total IgA in saliva was assessed using enzyme-linked immunosorbent assay (ELISA).

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

End point timeframe:

Day 0 (pre-vaccination) and Day 10, 14, 21, and 180 post-vaccination

Notes:

[10] - 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** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| D10/D0 | 0.962 (0.707 to 1.31) | 1.39 (1.02 to 1.92) | 0.909 (0.699 to 1.18) | 0.701 (0.364 to 1.35) |
| D14/D0 | 0.872 (0.671 to 1.13) | 1.18 (0.659 to 2.1) | 1.04 (0.823 to 1.32) | 0.816 (0.603 to 1.1) |
| D21/D0 | 0.95 (0.736 to 1.23) | 0.887 (0.418 to 1.88) | 0.941 (0.639 to 1.39) | 0.76 (0.506 to 1.14) |
| D180/D0 | 1.08 (0.521 to 2.22) | 1.06 (0.486 to 2.32) | 0.614 (0.246 to 1.53) | 0.39 (0.134 to 1.13) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers of Influenza-specific IgA in Saliva of Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| End point title | Geometric Mean Titers of Influenza-specific IgA in Saliva of Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[11] |
|---|---|

End point description:

Influenza-specific IgA in saliva was assessed using enzyme-linked immunosorbent assay (ELISA).

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

End point timeframe:

Day 0 (pre-vaccination) and Day 10, 14, 21, and 180 post-vaccination

Notes:

[11] - 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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titer (AU) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| D0 | 0.058 (0.027 to 0.124) | 0.014 (0.006 to 0.035) | 0.011 (0.004 to 0.027) | 0.014 (0.005 to 0.039) |
| D10 | 0.064 (0.029 to 0.141) | 0.041 (0.018 to 0.094) | 0.041 (0.015 to 0.108) | 0.029 (0.01 to 0.079) |
| D14 | 0.078 (0.037 to 0.163) | 0.025 (0.01 to 0.064) | 0.039 (0.015 to 0.106) | 0.046 (0.02 to 0.104) |
| D21 | 0.044 (0.021 to 0.095) | 0.058 (0.029 to 0.115) | 0.048 (0.023 to 0.101) | 0.015 (0.006 to 0.039) |
| D180 | 0.02 (0.007 to 0.057) | 0.021 (0.009 to 0.05) | 0.025 (0.008 to 0.075) | 0.017 (0.006 to 0.051) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers Ratios of Influenza-specific IgA in Saliva of Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route

| End point title | Geometric Mean Titers Ratios of Influenza-specific IgA in Saliva of Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Intradermal or Intramuscular Route[12] |
|---|---|

End point description:

Influenza-specifc IgA in saliva was assessed using enzyme-linked immunosorbent assay (ELISA).

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

End point timeframe:

Day 0 (pre-vaccination) and Day 10, 14, 21, and 180 post-vaccination

Notes:

[12] - 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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| D10/D0 | 1.19 (0.544 to 2.62) | 2.87 (1.33 to 6.16) | 4.83 (1.56 to 15) | 2.38 (0.789 to 7.15) |
| D14/D0 | 1.35 (0.602 to 3.02) | 1.33 (0.615 to 2.89) | 4.12 (1.38 to 12.3) | 3.3 (1.27 to 8.62) |
| D21/D0 | 0.664 (0.245 to 1.8) | 4.12 (1.7 to 9.96) | 4.54 (1.91 to 10.8) | 1.11 (0.424 to 2.91) |
| D180/D0 | 0.361 (0.115 to 1.13) | 1.56 (0.402 to 6.04) | 2.31 (0.662 to 8.06) | 1.13 (0.285 to 4.53) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects With At Least One Solicited Reaction Listed in the CPMP NfG Within 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or by Intramuscular Route

| End point title | Percentage of Subjects With At Least One Solicited Reaction Listed in the CPMP NfG Within 3 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or by Intramuscular Route[13] |
|---|---|

End point description:

Solicited injection site reactions: Injection site induration >5 cm for >3 days and Injection site ecchymosis. Solicited systemic reactions: Pyrexia (rectal temperature > 38°C) for ≥24 hours, Malaise, and Shivering.

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

End point timeframe:

Day 0 up to Day 3 post-vaccination

Notes:

[13] - 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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| At least 1 reaction listed in CPMP recommendations | 37.8 | 26.2 | 12.5 | 17.5 |
| Injection site induration >5 cm for >3 days | 0 | 0 | 0 | 0 |
| Injection site ecchymosis | 10.8 | 9.5 | 2.5 | 7.5 |
| Pyrexia (rectal temperature > 38°C) for ≥24 hours | 2.7 | 7.1 | 2.5 | 0 |
| Malaise | 18.9 | 7.1 | 5 | 5 |
| Shivering | 18.9 | 11.9 | 5 | 7.5 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Ratios of Cytokine Secreting CD4 T Cells Post/Pre-Vaccination Ratio in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Either Intradermal or Intramuscular Route

| End point title | Geometric Mean Ratios of Cytokine Secreting CD4 T Cells Post/Pre-Vaccination Ratio in Adults and Elderly Subjects Vaccinated with an Inactivated Influenza Vaccine Administered By Either Intradermal or Intramuscular Route[14] |
|---|---|

End point description:

Cellular immune response was assessed using the intracellular cytokine staining (ICS) method.

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

End point timeframe:

Day 0 (pre-vaccination) and Day 7, 10, 14, 21, and 180 post-vaccination

Notes:

[14] - 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** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| IFN-γ+; A/H1N1 Solomon Island (D7/D0) | 1.03 (0.878 to 1.22) | 1.26 (0.92 to 1.72) | 1.23 (0.874 to 1.74) | 1.99 (1.34 to 2.94) |
| IFN-γ+; A/H3N2 Wisconsin (D7/D0) | 0.867 (0.733 to 1.03) | 0.852 (0.676 to 1.07) | 0.908 (0.732 to 1.13) | 1.21 (0.903 to 1.62) |
| IFN-γ+; B/Malaysia (D7/D0) | 1.02 (0.799 to 1.3) | 1.16 (0.912 to 1.48) | 1.08 (0.805 to 1.44) | 1.66 (1.08 to 2.57) |
| IFN-γ+; A/H1N1 Solomon Island (D10/D0) | 1.23 (0.953 to 1.6) | 1.05 (0.777 to 1.42) | 1.24 (0.937 to 1.63) | 1.22 (0.849 to 1.76) |
| IFN-γ+; A/H3N2 Wisconsin (D10/D0) | 1.01 (0.812 to 1.26) | 1 (0.859 to 1.17) | 1.02 (0.8 to 1.31) | 1.26 (0.985 to 1.62) |
| IFN-γ+; B/Malaysia (D10/D0) | 1.15 (0.935 to 1.42) | 1.29 (1.08 to 1.54) | 1.11 (0.869 to 1.41) | 1.43 (1.1 to 1.87) |
| IFN-γ+; A/H1N1 Solomon Island (D14/D0) | 1.08 (0.852 to 1.38) | 1.25 (0.974 to 1.61) | 1.19 (0.869 to 1.62) | 1.25 (0.98 to 1.6) |
| IFN-γ+; A/H3N2 Wisconsin (D14/D0) | 0.95 (0.828 to 1.09) | 0.937 (0.767 to 1.14) | 0.976 (0.762 to 1.25) | 1.18 (0.904 to 1.54) |
| IFN-γ+; B/Malaysia (D14/D0) | 1.13 (0.891 to 1.44) | 1.12 (0.902 to 1.38) | 1.02 (0.801 to 1.31) | 1.08 (0.763 to 1.52) |
| IFN-γ+; A/H1N1 Solomon Island (D21/D0) | 1.08 (0.833 to 1.4) | 1.12 (0.857 to 1.47) | 1.26 (0.83 to 1.92) | 1.34 (0.91 to 1.98) |
| IFN-γ+; A/H3N2 Wisconsin (D21/D0) | 0.903 (0.755 to 1.08) | 0.869 (0.679 to 1.11) | 1.11 (0.886 to 1.39) | 1.36 (1.08 to 1.72) |
| IFN-γ+; B/Malaysia (D21/D0) | 1.06 (0.871 to 1.29) | 1.11 (0.885 to 1.39) | 1.27 (1 to 1.62) | 1.27 (0.983 to 1.64) |
| IFN-γ+; A/H1N1 Solomon Island (D180/D0) | 1.5 (1.02 to 2.22) | 1.46 (0.972 to 2.2) | 1.07 (0.725 to 1.58) | 2 (1.45 to 2.75) |
| IFN-γ+; A/H3N2 Wisconsin (D180/D0) | 1.59 (1.23 to 2.07) | 1.39 (1.08 to 2.79) | 1.55 (1.05 to 2.27) | 1.76 (1.22 to 2.55) |
| IFN-γ+; B/Malaysia (D180/D0) | 1.27 (0.894 to 1.81) | 1.25 (0.944 to 1.66) | 1.36 (1.08 to 1.71) | 1.54 (1.05 to 2.27) |
| TNF-α+; A/H1N1 Solomon Island (D7/D0) | 0.722 (0.57 to 0.915) | 0.889 (0.689 to 1.15) | 0.879 (0.662 to 1.17) | 1.92 (1.37 to 2.7) |
| TNF-α+; A/H3N2 Wisconsin (D7/D0) | 0.907 (0.738 to 1.12) | 0.948 (0.739 to 1.22) | 0.929 (0.677 to 1.28) | 1.27 (0.927 to 1.73) |
| TNF-α+; B/Malaysia (D7/D0) | 0.996 (0.828 to 1.2) | 0.991 (0.837 to 1.17) | 1.01 (0.79 to 1.3) | 1.42 (0.895 to 2.25) |
| TNF-α+; A/H1N1 Solomon Island (D10/D0) | 0.945 (0.743 to 1.14) | 0.912 (0.777 to 1.07) | 0.957 (0.738 to 1.24) | 1.41 (1.05 to 1.9) |

| | | | | |
|---|---|---|---|---|
| TNF-α+; A/H3N2 Wisconsin (D10/D0) | 0.945 (0.735 to 1.22) | 1.23 (0.962 to 1.56) | 1.2 (0.88 to 1.64) | 0.971 (0.717 to 1.31) |
| TNF-α+; B/Malaysia (D10/D0) | 1.11 (0.918 to 1.35) | 1 (0.869 to 1.16) | 1.05 (0.879 to 1.25) | 1.26 (1.03 to 1.53) |
| TNF-α+; A/H1N1 Solomon Island (D14/D0) | 0.844 (0.66 to 1.08) | 0.988 (0.843 to 1.16) | 1.07 (0.839 to 1.37) | 1.33 (0.999 to 1.78) |
| TNF-α+; A/H3N2 Wisconsin (D14/D0) | 0.963 (0.738 to 1.26) | 0.918 (0.64 to 1.32) | 1.2 (0.895 to 1.61) | 1.48 (1.06 to 2.06) |
| TNF-α+; B/Malaysia (D14/D0) | 1.08 (0.891 to 1.3) | 1.06 (0.902 to 1.24) | 1.26 (0.963 to 1.64) | 1.1 (0.811 to 1.5) |
| TNF-α+; A/H1N1 Solomon Island (D21/D0) | 0.859 (0.694 to 1.06) | 0.961 (0.798 to 1.16) | 1.04 (0.774 to 1.39) | 1.05 (0.72 to 1.52) |
| TNF-α+; A/H3N2 Wisconsin (D21/D0) | 1.08 (0.758 to 1.54) | 1.03 (0.736 to 1.45) | 1.43 (1.06 to 1.94) | 1.45 (1.06 to 1.98) |
| TNF-α+; B/Malaysia (D21/D0) | 1.03 (0.848 to 1.24) | 1.07 (0.91 to 1.25) | 1.25 (1.05 to 1.48) | 1.21 (0.888 to 1.66) |
| TNF-α+; A/H1N1 Solomon Island (D180/D0) | 0.469 (0.344 to 0.64) | 0.689 (0.519 to 0.913) | 0.834 (0.524 to 1.33) | 1.43 (1.06 to 1.94) |
| TNF-α+; A/H3N2 Wisconsin (D180/D0) | 0.811 (0.539 to 1.22) | 0.92 (0.617 to 1.37) | 0.963 (0.545 to 1.7) | 1.45 (1.01 to 2.08) |
| TNF-α+; B/Malaysia (D180/D0) | 0.921 (0.649 to 1.31) | 1.01 (0.8 to 1.27) | 1.15 (0.829 to 1.61) | 1.89 (1.26 to 2.85) |
| IL-2+; A/H1N1 Solomon Island (D7/D0) | 0.701 (0.557 to 0.883) | 0.847 (0.629 to 1.14) | 0.976 (0.701 to 1.36) | 1.53 (1.19 to 1.96) |
| IL-2+; A/H3N2 Wisconsin (D7/D0) | 0.873 (0.66 to 1.15) | 0.985 (0.727 to 1.33) | 1.11 (0.834 to 1.49) | 1.41 (1.08 to 1.86) |
| IL-2+; B/Malaysia (D7/D0) | 0.955 (0.808 to 1.13) | 1.02 (0.738 to 1.4) | 0.931 (0.693 to 1.25) | 1.26 (0.917 to 1.72) |
| IL-2+; A/H1N1 Solomon Island (D10/D0) | 1.03 (0.794 to 1.33) | 1 (0.789 to 1.27) | 1.24 (0.876 to 1.74) | 1.55 (1.16 to 2.07) |
| IL-2+; A/H3N2 Wisconsin (D10/D0) | 0.696 (0.472 to 1.03) | 0.965 (0.742 to 1.25) | 1.22 (0.836 to 1.78) | 1.47 (1.09 to 1.98) |
| IL-2+; B/Malaysia (D10/D0) | 1.18 (0.943 to 1.47) | 1.2 (0.823 to 1.74) | 1.38 (1.04 to 1.84) | 1.47 (1.08 to 2) |
| IL-2+; A/H1N1 Solomon Island (D14/D0) | 1.06 (0.813 to 1.39) | 1.11 (0.886 to 1.4) | 1.34 (0.987 to 1.82) | 1.75 (1.28 to 2.4) |
| IL-2+; A/H3N2 Wisconsin (D14/D0) | 0.738 (0.491 to 1.11) | 1.13 (0.821 to 1.54) | 1.18 (0.774 to 1.81) | 1.68 (1.15 to 2.46) |
| IL-2+; B/Malaysia (D14/D0) | 1.3 (0.959 to 1.75) | 1.42 (1.08 to 1.88) | 1.55 (1.11 to 2.16) | 1.73 (1.21 to 2.47) |
| IL-2+; A/H1N1 Solomon Island (D21/D0) | 1.07 (0.854 to 1.33) | 1.11 (0.88 to 1.4) | 1.18 (0.793 to 1.76) | 1.76 (1.18 to 2.63) |
| IL-2+; A/H3N2 Wisconsin (D21/D0) | 0.875 (0.627 to 1.22) | 1.05 (0.746 to 1.48) | 1.2 (0.817 to 1.77) | 1.94 (1.3 to 2.9) |
| IL-2+; B/Malaysia (D21/D0) | 1.29 (1.03 to 1.6) | 1.59 (1.12 to 2.27) | 1.39 (0.991 to 1.95) | 1.82 (1.41 to 2.37) |
| IL-2+; A/H1N1 Solomon Island (D180/D0) | 0.899 (0.621 to 1.27) | 1.25 (0.956 to 1.64) | 1.28 (0.838 to 1.95) | 2.02 (1.56 to 2.6) |
| IL-2+; A/H3N2 Wisconsin (D180/D0) | 0.853 (0.584 to 1.24) | 1.1 (0.797 to 1.52) | 1.04 (0.633 to 1.71) | 1.76 (1.25 to 2.49) |
| IL-2+; B/Malaysia (D180/D0) | 1.21 (0.82 to 1.79) | 1.67 (1.2 to 2.33) | 1.43 (1.05 to 1.94) | 2.37 (1.65 to 3.41) |
| TNF-α+/IFN-γ+; A/H1N1 Solomon Island (D7/D0) | 1.14 (0.913 to 1.42) | 1.28 (0.891 to 1.85) | 1.33 (0.948 to 1.85) | 2.63 (1.71 to 4.04) |
| TNF-α+/IFN-γ+; A/H3N2 Wisconsin (D7/D0) | 0.987 (0.739 to 1.32) | 1.09 (0.789 to 1.51) | 1.2 (0.853 to 1.68) | 1.56 (1.02 to 2.4) |
| TNF-α+/IFN-γ+; B/Malaysia (D7/D0) | 1.16 (0.93 to 1.44) | 1.34 (1.04 to 1.73) | 1.18 (0.793 to 1.75) | 2.44 (1.36 to 4.36) |
| TNF-α+/IFN-γ+; A/H1N1 Solomon Island (D10/D0) | 0.98 (0.77 to 1.25) | 1.08 (0.816 to 1.43) | 0.912 (0.671 to 1.24) | 1.42 (1.1 to 1.83) |
| TNF-α+/IFN-γ+; A/H3N2 Wisconsin (D10/D0) | 1.07 (0.779 to 1.46) | 1.48 (1.08 to 2.02) | 1.43 (1.02 to 1.99) | 1.31 (0.949 to 1.81) |

| | | | | |
|---|---|---|---|---|
| TNF-α+/IFN-γ+; B/Malaysia (D10/D0) | 1.08 (0.9 to 1.3) | 1.13 (0.895 to 1.42) | 1.21 (0.912 to 1.6) | 1.87 (1.31 to 2.67) |
| TNF-α+/IFN-γ+; A/H1N1 Solomon Island (D14/D0) | 0.77 (0.565 to 1.05) | 1.17 (0.878 to 1.56) | 1.16 (0.929 to 1.46) | 1.66 (1.25 to 2.21) |
| TNF-α+/IFN-γ+; A/H3N2 Wisconsin (D14/D0) | 0.913 (0.69 to 1.21) | 1.13 (0.853 to 1.5) | 1.13 (0.753 to 1.68) | 1.55 (1.11 to 2.18) |
| TNF-α+/IFN-γ+; B/Malaysia (D14/D0) | 1.03 (0.825 to 1.3) | 1.18 (1.01 to 1.37) | 1.25 (0.846 to 1.84) | 1.47 (0.983 to 2.19) |
| TNF-α+/IFN-γ+; A/H1N1 Solomon Island (D21/D0) | 0.914 (0.767 to 1.09) | 1.1 (0.824 to 1.46) | 1.06 (0.752 to 1.49) | 1.46 (1.06 to 2) |
| TNF-α+/IFN-γ+; A/H3N2 Wisconsin (D21/D0) | 1.09 (0.806 to 1.47) | 1.06 (0.748 to 1.5) | 1.45 (1.03 to 2.04) | 1.72 (1.24 to 2.37) |
| TNF-α+/IFN-γ+; B/Malaysia (D21/D0) | 0.984 (0.789 to 1.23) | 1.23 (0.968 to 1.56) | 1.32 (0.922 to 1.89) | 1.74 (1.3 to 2.34) |
| TNF-α+/IFN-γ+; A/H1N1 Solomon Island (D180/D0) | 1.12 (0.838 to 1.49) | 1.61 (1.16 to 2.22) | 1.6 (1.18 to 2.19) | 2.13 (1.67 to 2.72) |
| TNF-α+/IFN-γ+; A/H3N2 Wisconsin (D180/D0) | 1.58 (1.04 to 2.41) | 1.66 (1.14 to 2.42) | 1.69 (1.08 to 2.66) | 2.22 (1.64 to 3.02) |
| TNF-α+/IFN-γ+; B/Malaysia (D180/D0) | 1.31 (0.971 to 1.76) | 1.45 (1.09 to 1.92) | 1.43 (1.06 to 1.94) | 2.14 (1.42 to 3.21) |
| IFN-γ+/IL-2+; A/H1N1 Solomon Island (D7/D0) | 0.815 (0.644 to 1.03) | 0.931 (0.704 to 1.23) | 1.06 (0.782 to 1.44) | 1.66 (1.3 to 2.13) |
| IFN-γ+/IL-2+; A/H3N2 Wisconsin (D7/D0) | 0.804 (0.624 to 1.04) | 1.09 (0.791 to 1.49) | 1.1 (0.845 to 1.42) | 0.997 (0.785 to 1.27) |
| IFN-γ+/IL-2+; B/Malaysia (D7/D0) | 0.783 (0.55 to 1.11) | 1.15 (0.869 to 1.52) | 0.795 (0.593 to 1.08) | 1.1 (0.876 to 1.38) |
| IFN-γ+/IL-2+; A/H1N1 Solomon Island (D10/D0) | 1.16 (0.888 to 1.51) | 1.08 (0.847 to 1.38) | 0.963 (0.706 to 1.31) | 1.37 (1.12 to 1.66) |
| IFN-γ+/IL-2+; A/H3N2 Wisconsin (D10/D0) | 0.91 (0.66 to 1.25) | 1.1 (0.872 to 1.39) | 0.998 (0.75 to 1.33) | 1.11 (0.866 to 1.43) |
| IFN-γ+/IL-2+; B/Malaysia (D10/D0) | 1.15 (0.863 to 1.54) | 1.06 (0.768 to 1.46) | 1.26 (0.909 to 1.76) | 1.11 (0.829 to 1.5) |
| IFN-γ+/IL-2+; A/H1N1 Solomon Island (D14/D0) | 1.05 (0.771 to 1.42) | 1.17 (0.859 to 1.59) | 1.25 (0.955 to 1.62) | 1.62 (1.22 to 2.15) |
| IFN-γ+/IL-2+; A/H3N2 Wisconsin (D14/D0) | 0.831 (0.58 to 1.19) | 1.01 (0.741 to 1.39) | 1.24 (0.911 to 1.68) | 1.56 (1.2 to 2.03) |
| IFN-γ+/IL-2+; B/Malaysia (D14/D0) | 1.09 (0.763 to 1.55) | 1.35 (1.02 to 1.79) | 1.19 (0.888 to 1.61) | 1.32 (0.988 to 1.75) |
| IFN-γ+/IL-2+; A/H1N1 Solomon Island (D21/D0) | 1.05 (0.804 to 1.38) | 1.04 (0.773 to 1.41) | 1.3 (0.907 to 1.87) | 1.69 (1.23 to 2.31) |
| IFN-γ+/IL-2+; A/H3N2 Wisconsin (D21/D0) | 0.969 (0.667 to 1.41) | 1.02 (0.721 to 1.46) | 1.17 (0.837 to 1.62) | 1.53 (1.14 to 2.04) |
| IFN-γ+/IL-2+; B/Malaysia (D21/D0) | 1.11 (0.822 to 1.5) | 1.5 (1.13 to 1.99) | 1.43 (1.03 to 1.99) | 1.51 (1.16 to 1.95) |
| IFN-γ+/IL-2+; A/H1N1 Solomon Island (D180/D0) | 1.23 (0.899 to 1.68) | 1.44 (1.05 to 1.96) | 1.52 (1.11 to 2.1) | 1.96 (1.58 to 2.42) |
| IFN-γ+/IL-2+; A/H3N2 Wisconsin (D180/D0) | 1.09 (0.725 to 1.64) | 1.27 (0.996 to 1.63) | 0.843 (0.599 to 1.19) | 1.51 (1.08 to 1.85) |
| IFN-γ+/IL-2+; B/Malaysia (D180/D0) | 1.25 (0.882 to 1.77) | 1.56 (1.1 to 2.21) | 1.08 (0.793 to 1.47) | 1.41 (1.19 to 1.91) |
| TNF-α+/IL-2+; A/H1N1 Solomon Island (D7/D0) | 0.566 (0.421 to 0.761) | 0.703 (0.526 to 0.941) | 0.69 (0.521 to 0.913) | 1.1 (0.822 to 1.47) |
| TNF-α+/IL-2+; A/H3N2 Wisconsin (D7/D0) | 0.719 (0.538 to 0.959) | 0.999 (0.766 to 1.3) | 0.934 (0.725 to 1.2) | 0.856 (0.672 to 1.09) |
| TNF-α+/IL-2+; B/Malaysia (D7/D0) | 0.785 (0.589 to 1.05) | 0.894 (0.689 to 1.16) | 0.729 (0.542 to 0.98) | 0.96 (0.743 to 1.24) |
| TNF-α+/IL-2+; A/H1N1 Solomon Island (D10/D0) | 0.894 (0.635 to 1.26) | 0.848 (0.648 to 1.11) | 1.08 (0.829 to 1.4) | 1.17 (0.912 to 1.51) |
| TNF-α+/IL-2+; A/H3N2 Wisconsin (D10/D0) | 0.787 (0.551 to 1.13) | 1.04 (0.803 to 1.34) | 1.17 (0.851 to 1.62) | 1.08 (0.798 to 1.46) |
| TNF-α+/IL-2+; B/Malaysia (D10/D0) | 1.09 (0.792 to 1.5) | 1 (0.703 to 1.42) | 1.27 (0.999 to 1.62) | 1.2 (0.881 to 1.65) |

| | | | | |
|---|---|---|---|---|
| TNF-α+/IL-2+; A/H1N1 Solomon Island (D14/D0) | 0.95 (0.696 to 1.3) | 0.935 (0.696 to 1.26) | 1.19 (0.865 to 1.64) | 1.53 (1.2 to 1.94) |
| TNF-α+/IL-2+; A/H3N2 Wisconsin (D14/D0) | 0.818 (0.597 to 1.12) | 1.01 (0.75 to 1.36) | 1.19 (0.853 to 1.65) | 1.24 (0.896 to 1.72) |
| TNF-α+/IL-2+; B/Malaysia (D14/D0) | 1.13 (0.784 to 1.63) | 1.48 (1.16 to 1.88) | 1.46 (1.08 to 1.98) | 1.44 (0.984 to 2.12) |
| TNF-α+/IL-2+; A/H1N1 Solomon Island (D21/D0) | 0.909 (0.68 to 1.21) | 1.01 (0.749 to 1.35) | 1.09 (0.763 to 1.55) | 1.53 (1.08 to 2.16) |
| TNF-α+/IL-2+; A/H3N2 Wisconsin (D21/D0) | 0.956 (0.712 to 1.28) | 0.929 (0.657 to 1.31) | 1.1 (0.808 to 1.5) | 1.44 (1.03 to 2.02) |
| TNF-α+/IL-2+; B/Malaysia (D21/D0) | 1.13 (0.813 to 1.57) | 1.5 (1.08 to 2.08) | 1.53 (1.23 to 1.89) | 1.74 (1.39 to 2.17) |
| TNF-α+/IL-2+; A/H1N1 Solomon Island (D180/D0) | 0.888 (0.614 to 1.28) | 1.28 (0.923 to 1.77) | 1.43 (0.971 to 2.1) | 1.96 (1.48 to 2.59) |
| TNF-α+/IL-2+; A/H3N2 Wisconsin (D180/D0) | 0.977 (0.711 to 1.34) | 1.12 (0.819 to 1.52) | 0.959 (0.639 to 1.44) | 1.2 (0.861 to 1.66) |
| TNF-α+/IL-2+; B/Malaysia (D180/D0) | 1.28 (0.971 to 1.9) | 1.61 (1.14 to 2.26) | 1.47 (1.12 to 1.93) | 2.55 (1.78 to 3.67) |
| IFN-γ+/TNF-α+/IL-2+; A/H1N1 Solomon Island (D7/D0) | 0.737 (0.568 to 0.956) | 0.826 (0.631 to 1.08) | 0.949 (0.692 to 1.3) | 1.23 (0.974 to 1.54) |
| IFN-γ+/TNF-α+/IL-2+; A/H3N2 Wisconsin (D7/D0) | 0.87 (0.677 to 1.12) | 1.2 (0.911 to 1.59) | 0.977 (0.785 to 1.22) | 0.875 (0.71 to 1.08) |
| IFN-γ+/TNF-α+/IL-2+; B/Malaysia (D7/D0) | 0.79 (0.586 to 1.06) | 0.993 (0.749 to 1.32) | 0.709 (0.544 to 0.925) | 0.828 (0.648 to 1.06) |
| IFN-γ+/TNF-α+/IL-2+;A/H1N1 Solomon Island (D10/D0) | 0.931 (0.706 to 1.23) | 0.977 (0.724 to 1.32) | 0.982 (0.725 to 1.33) | 1.06 (0.903 to 1.25) |
| IFN-γ+/TNF-α+/IL-2+; A/H3N2 Wisconsin (D10/D0) | 0.917 (0.66 to 1.27) | 1.21 (0.925 to 1.6) | 1.16 (0.873 to 1.53) | 1.11 (0.909 to 1.35) |
| IFN-γ+/TNF-α+/IL-2+; B/Malaysia (D10/D0) | 1.08 (0.805 to 1.45) | 1.04 (0.77 to 1.41) | 1.07 (0.876 to 1.31) | 1.17 (0.899 to 1.53) |
| IFN-γ+/TNF-α+/IL-2+;A/H1N1 Solomon Island (D14/D0) | 0.849 (0.663 to 1.09) | 1.04 (0.766 to 1.41) | 1.15 (0.883 to 1.51) | 1.51 (1.15 to 2) |
| IFN-γ+/TNF-α+/IL-2+; A/H3N2 Wisconsin (D14/D0) | 0.818 (0.604 to 1.11) | 0.992 (0.747 to 1.32) | 1.09 (0.842 to 1.41) | 1.14 (0.897 to 1.45) |
| IFN-γ+/TNF-α+/IL-2+; B/Malaysia (D14/D0) | 1.11 (0.805 to 1.53) | 1.53 (1.19 to 1.98) | 1.26 (0.989 to 1.61) | 1.28 (0.951 to 1.72) |
| IFN-γ+/TNF-α+/IL-2+;A/H1N1 Solomon Island (D21/D0) | 0.824 (0.626 to 1.08) | 0.932 (0.706 to 1.23) | 1.21 (0.91 to 1.61) | 1.46 (1.07 to 1.99) |
| IFN-γ+/TNF-α+/IL-2+; A/H3N2 Wisconsin (D21/D0) | 1.02 (0.745 to 1.39) | 0.983 (0.703 to 1.38) | 1.13 (0.919 to 1.4) | 1.42 (1.11 to 1.82) |
| IFN-γ+/TNF-α+/IL-2+; B/Malaysia (D21/D0) | 1.17 (0.881 to 1.55) | 1.45 (1.07 to 1.96) | 1.25 (0.955 to 1.63) | 1.78 (1.38 to 2.29) |
| IFN-γ+/TNF-α+/IL-2+;A/H1N1 Solomon Island; D180/D0 | 1.26 (0.908 to 1.74) | 1.61 (1.2 to 2.16) | 1.86 (1.39 to 2.49) | 2.04 (1.67 to 2.49) |
| IFN-γ+/TNF-α+/IL-2+; A/H3N2 Wisconsin (D180/D0) | 1.34 (0.931 to 1.92) | 1.29 (0.952 to 1.76) | 0.991 (0.764 to 1.29) | 1.2 (0.921 to 1.56) |
| IFN-γ+/TNF-α+/IL-2+; B/Malaysia (D180/D0) | 1.41 (0.94 to 2.12) | 1.63 (1.2 to 2.21) | 1.1 (0.839 to 1.44) | 1.59 (1.19 to 2.12) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With At Least One Solicited Injection-site and Systemic Reactions Within 7 Days After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or by Intramuscular Route

| | |
|---|---|
| End point title | Percentage of Subjects With At Least One Solicited Injection-site and Systemic Reactions Within 7 Days After Vaccination |

| | |
|---|---|
| | with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or by Intramuscular Route |

End point description:

Solicited injection site: Pain, Pruritus, Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 injection site: Pain and Pruritus – Incapacitating, unable to perform usual activities; Erythema, Swelling, Induration, and Ecchymosis – ≥5 cm. Grade 3 systemic reactions: Fever – ≥39.0°C; Headache, Malaise, Myalgia, and Shivering – Prevents daily activities.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Day 0 up to Day 7 post-vaccination

| **End point values** | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg | Elderly - IM 15µg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 38 | 42 | 40 | 40 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection site Pain | 59.5 | 73.8 | 32.5 | 27.5 |
| Grade 3 Injection site Pain | 0 | 0 | 0 | 0 |
| Injection site Pruritus | 56.8 | 26.2 | 55 | 25 |
| Grade 3 Injection site Pruritus | 0 | 0 | 0 | 0 |
| Injection site Erythema | 91.9 | 54.8 | 85 | 52.5 |
| Grade 3 Injection site Erythema | 59.5 | 16.7 | 25 | 20 |
| Injection site Swelling | 70.3 | 28.6 | 65 | 27.5 |
| Grade 3 Injection site Swelling | 10.8 | 9.5 | 5 | 0 |
| Injection site Induration | 91.9 | 52.4 | 90 | 47.5 |
| Grade 3 Injection site Induration | 13.5 | 14.3 | 0 | 0 |
| Injection site Ecchymosis | 21.6 | 9.5 | 5 | 7.5 |
| Grade 3 Injection site Ecchymosis | 0 | 0 | 0 | 0 |
| Fever | 10.8 | 11.9 | 5 | 0 |
| Grade 3 Fever | 0 | 2.4 | 0 | 0 |
| Headache | 51.4 | 50 | 20 | 25 |
| Grade 3 Headache | 2.7 | 2.4 | 0 | 0 |
| Malaise | 21.6 | 11.9 | 5 | 7.5 |
| Grade 3 Malaise | 2.7 | 4.8 | 0 | 0 |
| Myalgia | 40.5 | 33.3 | 22.5 | 22.5 |
| Grade 3 Myalgia | 2.7 | 4.8 | 0 | 0 |
| Shivering | 21.6 | 14.3 | 7.5 | 12.5 |
| Grade 3 Shivering | 2.7 | 4.8 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Adverse event data were collected form Day 0 (post-vaccination) up to Day 180 post-vaccination. | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 10.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Adult - ID 9µg |
| Reporting group description: | |
| Adults 18-40 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (9 µg). | |
| Reporting group title | Adult - IM 15µg |
| Reporting group description: | |
| Adults 18-40 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg). | |
| Reporting group title | Elderly - ID 15µg |
| Reporting group description: | |
| Elderly subjects 60-85 years of age who received the ID influenza vaccine (split-virion, inactivated), 2007-2008 Northern Hemisphere (NH) formulation (15 µg). | |
| Reporting group title | Elderly - IM 15µg |
| Reporting group description: | |
| Elderly subjects 60-85 years of age who received the IM influenza vaccine (split-virion, inactivated), 2007-2008 NH formulation (Vaxigrip®; 15 µg). | |

| Serious adverse events | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 42 (0.00%) | 1 / 40 (2.50%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastasis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 42 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 42 (0.00%) | 0 / 40 (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 |

| Serious adverse events | Elderly - IM 15µg | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastasis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 40 (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 | Adult - ID 9µg | Adult - IM 15µg | Elderly - ID 15µg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 34 / 38 (89.47%) | 31 / 42 (73.81%) | 36 / 40 (90.00%) |
| Nervous system disorders | | | |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[1] | 19 / 37 (51.35%) | 21 / 42 (50.00%) | 8 / 40 (20.00%) |
| occurrences (all) | 19 | 21 | 8 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed[2] | 2 / 37 (5.41%) | 1 / 42 (2.38%) | 1 / 40 (2.50%) |
| occurrences (all) | 2 | 1 | 1 |
| Injection site pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[3] | 22 / 37 (59.46%) | 31 / 42 (73.81%) | 13 / 40 (32.50%) |
| occurrences (all) | 22 | 31 | 13 |
| Injection site erythema | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[4] | 34 / 37 (91.89%) | 23 / 42 (54.76%) | 34 / 40 (85.00%) |
| occurrences (all) | 34 | 23 | 34 |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[5] | 26 / 37 (70.27%) | 12 / 42 (28.57%) | 26 / 40 (65.00%) |
| occurrences (all) | 26 | 12 | 26 |
| Injection site ecchymosis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[6] | 8 / 37 (21.62%) | 4 / 42 (9.52%) | 2 / 40 (5.00%) |
| occurrences (all) | 8 | 4 | 2 |
| Fever | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[7] | 4 / 37 (10.81%) | 5 / 42 (11.90%) | 2 / 40 (5.00%) |
| occurrences (all) | 4 | 5 | 2 |
| Malaise | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[8] | 8 / 37 (21.62%) | 5 / 42 (11.90%) | 2 / 40 (5.00%) |
| occurrences (all) | 8 | 5 | 2 |
| Shivering | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[9] | 8 / 37 (21.62%) | 6 / 42 (14.29%) | 3 / 40 (7.50%) |
| occurrences (all) | 8 | 6 | 3 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed[10] | 2 / 37 (5.41%) | 0 / 42 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 2 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Injection site pruritus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[11] | 21 / 37 (56.76%) | 11 / 42 (26.19%) | 22 / 40 (55.00%) |
| occurrences (all) | 21 | 11 | 22 |
| Injection site induration | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[12] | 34 / 37 (91.89%) | 22 / 42 (52.38%) | 36 / 40 (90.00%) |
| occurrences (all) | 34 | 22 | 36 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed[13] | 1 / 37 (2.70%) | 1 / 42 (2.38%) | 2 / 40 (5.00%) |
| occurrences (all) | 1 | 1 | 2 |
| Myalgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[14] | 15 / 37 (40.54%) | 14 / 42 (33.33%) | 9 / 40 (22.50%) |
| occurrences (all) | 15 | 14 | 9 |
| Infections and infestations | | | |
| Rhinitis | | | |
| subjects affected / exposed[15] | 2 / 37 (5.41%) | 1 / 42 (2.38%) | 1 / 40 (2.50%) |
| occurrences (all) | 2 | 1 | 1 |

| **Non-serious adverse events** | Elderly - IM 15µg | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 40 (52.50%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[1] | 10 / 40 (25.00%) | | |
| occurrences (all) | 40 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed[2] | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |
| Injection site pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[3] | 11 / 40 (27.50%) | | |
| occurrences (all) | 11 | | |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[4] | 21 / 40 (52.50%) | | |
| occurrences (all) | 21 | | |
| Injection site swelling | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[5] | 11 / 40 (27.50%) | | |
| occurrences (all) | 11 | | |
| Injection site ecchymosis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[6] | 3 / 40 (7.50%) | | |
| occurrences (all) | 3 | | |
| Fever | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[7] | 0 / 40 (0.00%) | | |
| occurrences (all) | 0 | | |
| Malaise | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[8] | 3 / 40 (7.50%) | | |
| occurrences (all) | 3 | | |
| Shivering | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[9] | 5 / 40 (12.50%) | | |
| occurrences (all) | 5 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed[10] | 0 / 40 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Injection site pruritus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[11] | 10 / 40 (25.00%) | | |
| occurrences (all) | 10 | | |
| Injection site induration | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[12] | 19 / 40 (47.50%) | | |
| occurrences (all) | 19 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Back pain<br>subjects affected / exposed[13]<br>occurrences (all)<br><br>Myalgia<br>alternative assessment type: Systematic<br>subjects affected / exposed[14]<br>occurrences (all) | 4 / 40 (10.00%)<br>4<br><br><br><br>9 / 40 (22.50%)<br>9 | | |
| Infections and infestations<br>Rhinitis<br>subjects affected / exposed[15]<br>occurrences (all) | 1 / 40 (2.50%)<br>1 | | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a unsolicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a unsolicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a unsolicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.
[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a unsolicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 18 December 2007 | Addressed observational objectives in order to further explore and document the influenza-specific B-cell response and B- and T-cell repertoires both qualitatively and quantitatively for each vaccine administered by the intradermal and intramuscular route |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported