



Clinical trial results:

A Pivotal Randomized, Single-Blind, Dose-Finding Study to Evaluate Immunogenicity, Safety and Tolerability of Different Formulations of an Adjuvanted and Non-Adjuvanted Egg-Derived, Inactivated Novel Swine Origin A/H1N1 Monovalent Subunit Influenza Virus Vaccine in Healthy Pediatric Subjects 3 to < 9 Years of Age

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-005106-38 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 03 November 2010 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 28 July 2016 |
| First version publication date | 09 May 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Required for the re-QC because of EudraCT system glitch as possible updates to results are required. Moreover, the study is now transferred to another primary user. |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | V112_02 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00972816 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Vaccines and Diagnostics |
| Sponsor organisation address | 350 Massachusetts Ave, Cambridge, MA, United States, 02139 |
| Public contact | Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com |
| Scientific contact | Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com |

Notes:

Paediatric regulatory details

| | |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 31 March 2011 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 November 2010 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To see if one or more A/H1N1 S-OIV vaccine groups meet CBER criteria for immunogenicity in a population of children aged 3 to < 9 yrs (CBER 2007)

Protection of trial subjects:

This trial was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines, the applicable regulatory requirements(s) for the country in which the study is conducted, and applicable standard operating procedures (SOPs).

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------------------|
| Actual start date of recruitment | 12 September 2009 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Regulatory reason |
| Long term follow-up duration | 13 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United States: 1357 |
| Worldwide total number of subjects | 1357 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 1357 |

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

Subject disposition

Recruitment

Recruitment details:

36 centers in the United States, of which 34 centers enrolled subjects

Pre-assignment

Screening details:

All enrolled subjects were included in the trial

Period 1

| | |
|------------------------------|---------------------------|
| Period 1 title | Enrolled (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Group A |

Arm description:

3.75_(50) MF59-[3.75 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22]

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine with MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.25mL dose/IM

| | |
|------------------|---------|
| Arm title | Group B |
|------------------|---------|

Arm description:

7.5_(0) MF59-[7.5 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22]

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine without MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.50 mL dose/IM

| | |
|------------------|---------|
| Arm title | Group C |
|------------------|---------|

Arm description:

7.5_(50) MF59-[7.5 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22]

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

| | |
|---|---|
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine with MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 0.50 mL dose/IM | |
| Arm title | Group D |
| Arm description: | |
| 7.5_(100) MF59-[7.5 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22] | |
| Arm type | Experimental |
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine with MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 0.50 mL dose/IM | |
| Arm title | Group E |
| Arm description: | |
| 15_(0) MF59-[15 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22] | |
| Arm type | Experimental |
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine without MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 0.50 mL dose/IM | |
| Arm title | Group F |
| Arm description: | |
| 15_(50) MF59-[15 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22] | |
| Arm type | Experimental |
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine with MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 0.50 mL dose/IM | |
| Arm title | Group G |
| Arm description: | |
| 15_(100) MF59-[15 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22] | |
| Arm type | Experimental |

| | |
|--|--|
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine with MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 0.50 mL dose/IM | |
| Arm title | Group H |

Arm description:

30_(0) MF59-[30 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22]

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Monovalent H1N1 influenza virus vaccine without MF59 adjuvant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.50 mL dose/IM

| Number of subjects in period 1 | Group A | Group B | Group C |
|---------------------------------------|---------|---------|---------|
| Started | 173 | 169 | 169 |
| Completed | 156 | 158 | 160 |
| Not completed | 17 | 11 | 9 |
| Consent withdrawn by subject | 4 | 2 | 1 |
| Adverse event, non-fatal | - | - | 1 |
| Unable to classify | 2 | - | - |
| Inappropriate enrolment | - | - | - |
| Lost to follow-up | 11 | 9 | 7 |

| Number of subjects in period 1 | Group D | Group E | Group F |
|---------------------------------------|---------|---------|---------|
| Started | 169 | 169 | 169 |
| Completed | 161 | 157 | 158 |
| Not completed | 8 | 12 | 11 |
| Consent withdrawn by subject | 3 | - | 1 |
| Adverse event, non-fatal | - | - | - |
| Unable to classify | - | 1 | - |
| Inappropriate enrolment | - | - | - |
| Lost to follow-up | 5 | 11 | 10 |

| Number of subjects in period 1 | Group G | Group H |
|---------------------------------------|---------|---------|
| Started | 169 | 170 |

| | | |
|------------------------------|-----|-----|
| Completed | 159 | 161 |
| Not completed | 10 | 9 |
| Consent withdrawn by subject | 1 | 2 |
| Adverse event, non-fatal | - | - |
| Unable to classify | - | - |
| Inappropriate enrolment | 2 | - |
| Lost to follow-up | 7 | 7 |

Baseline characteristics

| Reporting groups | |
|---|---------|
| Reporting group title | Group A |
| Reporting group description: 3.75_(50) MF59-[3.75 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group B |
| Reporting group description: 7.5_(0) MF59-[7.5 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group C |
| Reporting group description: 7.5_(50) MF59-[7.5 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group D |
| Reporting group description: 7.5_(100) MF59-[7.5 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group E |
| Reporting group description: 15_(0) MF59-[15 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group F |
| Reporting group description: 15_(50) MF59-[15 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group G |
| Reporting group description: 15_(100) MF59-[15 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group H |
| Reporting group description: 30_(0) MF59-[30 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22] | |

| Reporting group values | Group A | Group B | Group C |
|---|---------|---------|---------|
| Number of subjects | 173 | 169 | 169 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years arithmetic mean | 5.6 | 5.2 | 5.5 |

| | | | |
|--------------------|-------|-------|-------|
| standard deviation | ± 1.7 | ± 1.7 | ± 1.8 |
|--------------------|-------|-------|-------|

| | | | |
|---------------------------------------|----|----|----|
| Gender categorical Units: Subjects | | | |
| Female | 81 | 88 | 83 |
| Male | 92 | 81 | 86 |

| Reporting group values | Group D | Group E | Group F |
|--|---------|---------|---------|
| Number of subjects | 169 | 169 | 169 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 5.9 | 5.6 | 5.5 |
| standard deviation | ± 1.7 | ± 1.7 | ± 1.7 |
| Gender categorical Units: Subjects | | | |
| Female | 83 | 79 | 80 |
| Male | 86 | 90 | 89 |

| Reporting group values | Group G | Group H | Total |
|--|---------|---------|---|
| Number of subjects | 169 | 170 | 1357 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | 0 0 0 0 0 0 0 0 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 5.5 | 5.5 | - |
| standard deviation | ± 1.7 | ± 1.7 | - |

| | | | |
|--------------------|----|----|-----|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 75 | 83 | 652 |
| Male | 94 | 87 | 705 |

End points

End points reporting groups

| | |
|---|---------|
| Reporting group title | Group A |
| Reporting group description: 3.75_(50) MF59-[3.75 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group B |
| Reporting group description: 7.5_(0) MF59-[7.5 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group C |
| Reporting group description: 7.5_(50) MF59-[7.5 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group D |
| Reporting group description: 7.5_(100) MF59-[7.5 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group E |
| Reporting group description: 15_(0) MF59-[15 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group F |
| Reporting group description: 15_(50) MF59-[15 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group G |
| Reporting group description: 15_(100) MF59-[15 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22] | |
| Reporting group title | Group H |
| Reporting group description: 30_(0) MF59-[30 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22] | |

Primary: 1. Antibody Responses After the First and Second Vaccinations

| | |
|---|--|
| End point title | 1. Antibody Responses After the First and Second |
| End point description: CBER guidance (<65 years of age): The lower bound of the two-sided 95% CI for the percentages of subjects achieving seroconversion for HI antibody should be $\geq 40\%$ and the lower bound of the two-sided 95% CI for the percentages of subjects achieving an HI antibody titer $\geq 1:40$ should be $\geq 70\%$. PPS Day 1–29 analysis set. N= 143, 149, 149, 146, 147, 147, 144, and 144 for Groups A, B, C, D, E, F, G, and H, respectively. PPS Day 1–202 analysis set. N= 82, 85, 84, 84, 86, 87, 82, and 79 for Groups A, B, C, D, E, F, G, and H, respectively. PPS Day 1–387 analysis set. N= 55, 63, 61, 58, 61, 65, 59, and 63 for Groups A, B, C, D, E, F, G, and H, respectively. | |
| End point type | Primary |
| End point timeframe: Day 22, Day 29, Day 43, Day 202 and Day 387 | |
| 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: No statistical analyses for this end point. | |

| End point values | Group A | Group B | Group C | Group D |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 152 | 156 | 156 | 156 |
| Units: Percentages of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| HI titer $\geq 1:40$ (Baseline) | 11 (6 to 17) | 9 (5 to 15) | 13 (8 to 19) | 11 (6 to 17) |
| HI titer $\geq 1:40$ (Day 22) | 84 (77 to 89) | 48 (40 to 56) | 81 (74 to 87) | 91 (85 to 95) |
| Seroconversion (Day 22) | 82 (74 to 87) | 46 (38 to 54) | 78 (70 to 84) | 88 (82 to 93) |
| HI titer $\geq 1:40$ (Day 29) | 99 (96 to 100) | 79 (71 to 85) | 100 (98 to 100) | 99 (95 to 100) |
| Seroconversion (Day 29) | 99 (95 to 100) | 78 (70 to 84) | 99 (95 to 100) | 99 (95 to 100) |
| HI titer $\geq 1:40$ (Day 43) | 99 (96 to 100) | 79 (72 to 85) | 100 (98 to 100) | 99 (95 to 100) |
| Seroconversion (Day 43) | 98 (94 to 100) | 78 (70 to 84) | 97 (93 to 99) | 97 (94 to 99) |
| HI titer $\geq 1:40$ (Day 202) | 95 (88 to 99) | 65 (54 to 75) | 93 (85 to 97) | 95 (88 to 99) |
| Seroconversion (Day 202) | 83 (73 to 90) | 55 (44 to 66) | 83 (74 to 91) | 83 (74 to 91) |
| HI titer $\geq 1:40$ (Day 387) | 80 (67 to 90) | 56 (42 to 68) | 75 (63 to 86) | 88 (77 to 95) |
| Seroconversion (Day 387) | 65 (51 to 78) | 49 (36 to 62) | 69 (56 to 80) | 78 (65 to 87) |

| End point values | Group E | Group F | Group G | Group H |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 155 | 157 | 156 | 153 |
| Units: Percentages of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| HI titer $\geq 1:40$ (Baseline) | 15 (10 to 22) | 9 (5 to 15) | 8 (4 to 13) | 12 (8 to 19) |
| HI titer $\geq 1:40$ (Day 22) | 61 (52 to 68) | 82 (75 to 88) | 94 (89 to 97) | 65 (57 to 73) |
| Seroconversion (Day 22) | 58 (50 to 66) | 82 (75 to 87) | 92 (86 to 95) | 60 (52 to 68) |
| HI titer $\geq 1:40$ (Day 29) | 88 (82 to 93) | 100 (98 to 100) | 100 (97 to 100) | 97 (92 to 99) |
| Seroconversion (Day 29) | 87 (81 to 92) | 100 (98 to 100) | 100 (97 to 100) | 94 (88 to 97) |
| HI titer $\geq 1:40$ (Day 43) | 87 (81 to 92) | 99 (97 to 100) | 100 (98 to 100) | 92 (86 to 95) |
| Seroconversion (Day 43) | 85 (78 to 90) | 99 (95 to 100) | 99 (96 to 100) | 88 (82 to 93) |
| HI titer $\geq 1:40$ (Day 202) | 74 (64 to 83) | 95 (89 to 99) | 95 (88 to 99) | 81 (71 to 89) |
| Seroconversion (Day 202) | 63 (52 to 73) | 90 (81 to 95) | 90 (82 to 96) | 66 (54 to 76) |
| HI titer $\geq 1:40$ (Day 387) | 49 (36 to 62) | 78 (67 to 88) | 81 (69 to 90) | 65 (52 to 77) |
| Seroconversion (Day 387) | 44 (32 to 58) | 75 (63 to 85) | 71 (58 to 82) | 51 (38 to 64) |

Statistical analyses

No statistical analyses for this end point

Secondary: 2. Geometric Mean Titer After Each Vaccination by Vaccine Group

| | |
|-----------------|---|
| End point title | 2. Geometric Mean Titer After Each Vaccination by Vaccine Group |
|-----------------|---|

End point description:

Immunogenicity was measured in terms of GMTs After Each Vaccination by Vaccine Group.

PPS Day1–29 analysis set. N=143, 149, 149, 146, 147, 147, 144, and 144 for Groups A, B, C, D, E, F, G, and H, respectively.

PPS Day 1–202 analysis set. N= 82, 85, 84, 84, 86, 87, 82, and 79 for Groups A, B, C, D, E, F, G, and H, respectively.

PPS Day 1–387 analysis set. N= 55, 63, 61, 58, 61, 65, 59, and 63 for Groups A, B, C, D, E, F, G, and H, respectively.

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

End point timeframe:

Day 22, Day 29, Day 43, Day 202 and Day 387

| End point values | Group A | Group B | Group C | Group D |
|--|------------------|------------------|------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 152 | 156 | 156 | 156 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| GMT Baseline | 8.5 (7 to 10) | 7.3 (6 to 8.8) | 8.7 (7.2 to 11) | 8.1 (6.7 to 9.9) |
| GMT Day 22 | 107 (78 to 148) | 27 (20 to 37) | 88 (64 to 121) | 163 (118 to 223) |
| GMT Day 29 | 747 (588 to 950) | 138 (109 to 174) | 685 (542 to 866) | 984 (775 to 1249) |
| GMT Day 43 | 560 (450 to 699) | 113 (91 to 140) | 480 (386 to 597) | 637 (511 to 793) |
| GMT Day 202 | 117 (88 to 157) | 45 (34 to 59) | 107 (80 to 144) | 132 (99 to 177) |
| GMT Day 387 | 54 (37 to 78) | 28 (20 to 40) | 57 (40 to 82) | 70 (49 to 102) |

| End point values | Group E | Group F | Group G | Group H |
|--|------------------|------------------|--------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 155 | 157 | 156 | 153 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| GMT Baseline | 9.1 (7.5 to 11) | 7.5 (6.2 to 9.1) | 7 (5.8 to 8.4) | 9.1 (7.5 to 11) |
| GMT Day 22 | 49 (36 to 68) | 106 (77 to 145) | 160 (116 to 220) | 62 (45 to 85) |
| GMT Day 29 | 214 (169 to 271) | 761 (600 to 966) | 1070 (841 to 1360) | 297 (235 to 377) |
| GMT Day 43 | 174 (140 to 217) | 524 (420 to 652) | 778 (625 to 969) | 223 (179 to 278) |
| GMT Day 202 | 55 (41 to 74) | 134 (100 to 179) | 131 (97 to 176) | 81 (60 to 109) |
| GMT Day 387 | 30 (21 to 42) | 59 (41 to 83) | 63 (44 to 90) | 45 (31 to 64) |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | 1. GMT After Each Vaccination by Vaccine Group |
|----------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|--------------------------------|
| Comparison groups | Group A v Group B |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 3.998 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.659 |
| upper limit | 6.009 |

Notes:

[2] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 2. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|--------------------------------|
| Comparison groups | Group A v Group C |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.222 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.813 |
| upper limit | 1.838 |

Notes:

[3] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 3. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group A v Group D |
|-------------------|-------------------|

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[4] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.661 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 0.994 |

Notes:

[4] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 4. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|--------------------------------|
| Comparison groups | Group A v Group E |
| Number of subjects included in analysis | 307 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[5] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 2.178 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.449 |
| upper limit | 3.276 |

Notes:

[5] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 5.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|--------------------------------|
| Comparison groups | Group A v Group F |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[6] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.017 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.676 |
| upper limit | 1.528 |

Notes:

[6] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 6.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|--------------------------------|
| Comparison groups | Group A v Group G |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[7] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.673 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.448 |
| upper limit | 1.012 |

Notes:

[7] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 7.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|--------------------------------|
| Comparison groups | Group A v Group H |
| Number of subjects included in analysis | 305 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[8] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.742 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.156 |
| upper limit | 2.626 |

Notes:

[8] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 8.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|--------------------------------|
| Comparison groups | Group B v Group C |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[9] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.306 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.204 |
| upper limit | 0.458 |

Notes:

[9] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 9.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[10] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.165 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.11 |
| upper limit | 0.248 |

Notes:

[10] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 10.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group E v Group B |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[11] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.545 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.363 |
| upper limit | 0.818 |

Notes:

[11] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 11.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[12] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.254 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.17 |
| upper limit | 0.381 |

Notes:

[12] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 12.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[13] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.168 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.112 |
| upper limit | 0.252 |

Notes:

[13] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 13.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[14] |
| Method | ANOVA |
| Parameter estimate | Geometric.Mean Ratio at day 22 |
| Point estimate | 0.436 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 0.655 |

Notes:

[14] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 14.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group C |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[15] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.541 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.361 |
| upper limit | 0.811 |

Notes:

[15] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 15.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[16] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.783 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.188 |
| upper limit | 2.676 |

Notes:

[16] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 16.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[17] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.832 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.555 |
| upper limit | 1.246 |

Notes:

[17] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 17.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group C v Group G |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[18] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.551 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.367 |
| upper limit | 0.826 |

Notes:

[18] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 18.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[19] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.426 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 2.14 |

Notes:

[19] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 19.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[20] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 3.295 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.196 |
| upper limit | 4.944 |

Notes:

[20] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 20. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[21] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.538 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.026 |
| upper limit | 2.303 |

Notes:

[21] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 21. GMT After Each Vaccination by Vaccination |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[22] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.018 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.679 |
| upper limit | 1.526 |

Notes:

[22] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 22. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[23] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 2.635 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.754 |
| upper limit | 3.959 |

Notes:

[23] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 23. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group F v Group E |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[24] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.467 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.311 |
| upper limit | 0.7 |

Notes:

[24] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 24. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group E v Group G |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[25] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.309 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.206 |
| upper limit | 0.463 |

Notes:

[25] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 26. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group F v Group G |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[26] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.662 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.442 |
| upper limit | 0.992 |

Notes:

[26] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 27. GMT After Each Vaccination by Vaccination |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group H v Group F |
| Number of subjects included in analysis | 310 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[27] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 1.714 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.142 |
| upper limit | 2.572 |

Notes:

[27] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 28. GMT After Each Vaccination by Vaccination |
|-----------------------------------|---|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group H v Group G |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[28] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 2.589 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.723 |
| upper limit | 3.889 |

Notes:

[28] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 29. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group B |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[29] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 5.428 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4 |
| upper limit | 7.365 |

Notes:

[29] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|---|
| Statistical analysis title | 30. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group C |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[30] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 1.091 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.804 |
| upper limit | 1.481 |

Notes:

[30] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 31.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group D |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[31] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.759 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.559 |
| upper limit | 1.031 |

Notes:

[31] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 32.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group A v Group E |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 307 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[32] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 3.499 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.577 |
| upper limit | 4.751 |

Notes:

[32] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 33.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group F |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[33] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.982 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.722 |
| upper limit | 1.334 |

Notes:

[33] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 34.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group G |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[34] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.699 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.513 |
| upper limit | 0.95 |

Notes:

[34] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 35.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group H |
| Number of subjects included in analysis | 305 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[35] |
| Method | ANOVA |
| Parameter estimate | GMR at day 29 |
| Point estimate | 2.513 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.846 |
| upper limit | 3.421 |

Notes:

[35] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 36.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group C |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[36] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.201 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.149 |
| upper limit | 0.272 |

Notes:

[36] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 37.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[37] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.103 |
| upper limit | 0.189 |

Notes:

[37] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 38.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[38] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.645 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.476 |
| upper limit | 0.873 |

Notes:

[38] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 39.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group B v Group F |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[39] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.181 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.134 |
| upper limit | 0.245 |

Notes:

[39] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 40.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[40] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.129 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.095 |
| upper limit | 0.174 |

Notes:

[40] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 41.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[41] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.463 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.341 |
| upper limit | 0.628 |

Notes:

[41] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 42.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[42] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.696 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.514 |
| upper limit | 0.943 |

Notes:

[42] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 43.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group E v Group C |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[43] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 3.207 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.368 |
| upper limit | 4.343 |

Notes:

[43] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 44.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[44] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.665 |
| upper limit | 1.218 |

Notes:

[44] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 45.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[45] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.472 |
| upper limit | 0.868 |

Notes:

[45] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 46.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group C v Group H |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[46] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 2.303 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.7 |
| upper limit | 3.121 |

Notes:

[46] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 47.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[47] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 4.608 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.398 |
| upper limit | 6.249 |

Notes:

[47] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 48.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[48] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 1.293 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.954 |
| upper limit | 1.753 |

Notes:

[48] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 49.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[49] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.677 |
| upper limit | 1.249 |

Notes:

[49] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 50.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group H v Group D |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[50] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 3.31 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.436 |
| upper limit | 4.496 |

Notes:

[50] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 51.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group E v Group F |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[51] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.281 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.207 |
| upper limit | 0.38 |

Notes:

[51] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 52.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group E v Group G |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[52] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.147 |
| upper limit | 0.271 |

Notes:

[52] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 53.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group H v Group E |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[53] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.718 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.529 |
| upper limit | 0.975 |

Notes:

[53] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 54.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group F v Group G |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[54] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 0.712 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.524 |
| upper limit | 0.966 |

Notes:

[54] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 55.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group H v Group F |
| Number of subjects included in analysis | 310 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[55] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 2.56 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.886 |
| upper limit | 3.474 |

Notes:

[55] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 56.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 29-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group H v Group G |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[56] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 29 |
| Point estimate | 3.597 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.646 |
| upper limit | 4.89 |

Notes:

[56] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 57.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group A |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[57] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 4.975 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.757 |
| upper limit | 6.589 |

Notes:

[57] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 58.GMT After Each Vaccination by Vaccination |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group C |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[58] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 1.168 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.881 |
| upper limit | 1.547 |

Notes:

[58] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 59.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group D |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[59] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.665 |
| upper limit | 1.166 |

Notes:

[59] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 60.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group A v Group E |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 307 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[60] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 3.219 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.43 |
| upper limit | 4.264 |

Notes:

[60] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 61.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group F |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[61] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 1.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.808 |
| upper limit | 1.417 |

Notes:

[61] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 62.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group G |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[62] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.72 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.544 |
| upper limit | 0.954 |

Notes:

[62] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 63.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group H |
| Number of subjects included in analysis | 305 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[63] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 2.509 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.891 |
| upper limit | 3.33 |

Notes:

[63] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 64.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group B |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[64] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.235 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.178 |
| upper limit | 0.31 |

Notes:

[64] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|---|
| Statistical analysis title | 65. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[65] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.177 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.134 |
| upper limit | 0.234 |

Notes:

[65] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 66.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[66] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.647 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.489 |
| upper limit | 0.856 |

Notes:

[66] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|---|
| Statistical analysis title | 67. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group B v Group F |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[67] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.215 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.163 |
| upper limit | 0.284 |

Notes:

[67] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 68.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[68] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.145 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.109 |
| upper limit | 0.191 |

Notes:

[68] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 69.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[69] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.504 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.381 |
| upper limit | 0.668 |

Notes:

[69] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 70.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[70] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.754 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.57 |
| upper limit | 0.997 |

Notes:

[70] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|---|
| Statistical analysis title | 71.GMTAfter Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[71] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 2.756 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.083 |
| upper limit | 3.647 |

Notes:

[71] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|---|
| Statistical analysis title | 72. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[72] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.916 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.694 |
| upper limit | 1.211 |

Notes:

[72] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 73.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[73] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.616 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.466 |
| upper limit | 0.815 |

Notes:

[73] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 74.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group C v Group H |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[74] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 2.149 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.624 |
| upper limit | 2.843 |

Notes:

[74] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 75.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[75] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 3.656 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.764 |
| upper limit | 4.836 |

Notes:

[75] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 76.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[76] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 1.216 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.92 |
| upper limit | 1.606 |

Notes:

[76] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 77.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[77] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.818 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.619 |
| upper limit | 1.081 |

Notes:

[77] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|---|
| Statistical analysis title | 78.GMTAfter Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group D v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[78] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 2.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.152 |
| upper limit | 3.773 |

Notes:

[78] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 79.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group E v Group F |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[79] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.332 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.251 |
| upper limit | 0.44 |

Notes:

[79] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 80.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group E v Group G |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[80] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.224 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.169 |
| upper limit | 0.296 |

Notes:

[80] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 81.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group E v Group H |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[81] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.588 |
| upper limit | 1.033 |

Notes:

[81] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 82.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group F v Group G |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[82] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 0.673 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.509 |
| upper limit | 0.889 |

Notes:

[82] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 83.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group F v Group H |
| Number of subjects included in analysis | 310 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[83] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 2.345 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.772 |
| upper limit | 3.102 |

Notes:

[83] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 84.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 43-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group G v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[84] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 43 |
| Point estimate | 3.485 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.633 |
| upper limit | 4.614 |

Notes:

[84] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

| | |
|-----------------------------------|--|
| Statistical analysis title | 85.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group B |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[85] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 2.624 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.817 |
| upper limit | 3.789 |

Notes:

[85] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 86.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group C |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[86] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.096 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.58 |

Notes:

[86] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 87.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group D |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[87] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.888 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.615 |
| upper limit | 1.282 |

Notes:

[87] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 88.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group A v Group E |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 307 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[88] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 2.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.473 |
| upper limit | 3.052 |

Notes:

[88] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 89.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group F |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[89] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.876 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 1.26 |

Notes:

[89] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 90.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group G |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[90] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.898 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.622 |
| upper limit | 1.298 |

Notes:

[90] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 91.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group A v Group H |
| Number of subjects included in analysis | 305 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[91] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.451 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 2.105 |

Notes:

[91] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 92.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group C |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[92] |
| Method | ANOVA |
| Parameter estimate | Geometric.Mean Ratio at day 202 |
| Point estimate | 0.418 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.289 |
| upper limit | 0.603 |

Notes:

[92] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 93.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[93] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.338 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.235 |
| upper limit | 0.487 |

Notes:

[93] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 94.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[94] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.808 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.561 |
| upper limit | 1.165 |

Notes:

[94] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 95.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group B v Group F |
|-------------------|-------------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[95] |
| Method | ANOVA |
| Parameter estimate | Geometric.Mean Ratio at day 202 |
| Point estimate | 0.334 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.233 |
| upper limit | 0.479 |

Notes:

[95] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 96.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[96] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.342 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.237 |
| upper limit | 0.494 |

Notes:

[96] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 97.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group B v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[97] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.553 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.382 |
| upper limit | 0.801 |

Notes:

[97] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 98.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[98] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.811 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.562 |
| upper limit | 1.169 |

Notes:

[98] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 99.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|---------------------------------|
| Comparison groups | Group C v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[99] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.935 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.347 |
| upper limit | 2.78 |

Notes:

[99] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 100.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group C v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[100] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.558 |
| upper limit | 1.147 |

Notes:

[100] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 101.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group C v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[101] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.568 |
| upper limit | 1.184 |

Notes:

[101] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 102.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group C v Group H |
|-------------------|-------------------|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[102] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.324 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.915 |
| upper limit | 1.917 |

Notes:

[102] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 103.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group D v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[103] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 2.388 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.658 |
| upper limit | 3.438 |

Notes:

[103] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 104.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group D v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[104] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.987 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.688 |
| upper limit | 1.416 |

Notes:

[104] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 105.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group D v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[105] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.012 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.701 |
| upper limit | 1.46 |

Notes:

[105] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 106.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group H v Group D |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[106] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.634 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.128 |
| upper limit | 2.366 |

Notes:

[106] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 107.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group E v Group F |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[107] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.413 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.288 |
| upper limit | 0.592 |

Notes:

[107] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 108. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group E v Group G |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[108] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.424 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.294 |
| upper limit | 0.61 |

Notes:

[108] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 109. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group E v Group H |
|-------------------|-------------------|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[109] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 0.684 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.473 |
| upper limit | 0.99 |

Notes:

[109] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 110.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group F v Group G |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[110] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.025 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.714 |
| upper limit | 1.473 |

Notes:

[110] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 111.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group F v Group H |
| Number of subjects included in analysis | 310 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[111] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.656 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.15 |
| upper limit | 2.385 |

Notes:

[111] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 112.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 202-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group G v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[112] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 202 |
| Point estimate | 1.615 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.115 |
| upper limit | 2.339 |

Notes:

[112] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 113.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group A v Group B |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[113] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.906 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.177 |
| upper limit | 3.087 |

Notes:

[113] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 114.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group A v Group C |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[114] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.945 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.583 |
| upper limit | 1.533 |

Notes:

[114] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 115. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group A v Group D |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[115] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.763 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.468 |
| upper limit | 1.245 |

Notes:

[115] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 116. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group A v Group E |
|-------------------|-------------------|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 307 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[116] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.818 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.119 |
| upper limit | 2.956 |

Notes:

[116] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 117.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group A v Group F |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[117] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.917 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.568 |
| upper limit | 1.481 |

Notes:

[117] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 118. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group A v Group G |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[118] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.855 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.524 |
| upper limit | 1.396 |

Notes:

[118] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 119. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group A v Group H |
| Number of subjects included in analysis | 305 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[119] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.203 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.745 |
| upper limit | 1.943 |

Notes:

[119] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 120. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group B v Group C |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[120] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.496 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.31 |
| upper limit | 0.794 |

Notes:

[120] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 121. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group B v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[121] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 0.641 |

Notes:

[121] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 122.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group B v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[122] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.954 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.596 |
| upper limit | 1.528 |

Notes:

[122] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 123.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group B v Group F |
|-------------------|-------------------|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[123] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.481 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.306 |
| upper limit | 0.758 |

Notes:

[123] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 124.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group G v Group B |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[124] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.449 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.279 |
| upper limit | 0.722 |

Notes:

[124] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 125.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group B v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[125] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.631 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.398 |
| upper limit | 1.002 |

Notes:

[125] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 126.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group C v Group D |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[126] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.807 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 1.304 |

Notes:

[126] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 127.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group C v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[127] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.924 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.193 |
| upper limit | 3.102 |

Notes:

[127] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 128.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group C v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[128] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.611 |
| upper limit | 1.541 |

Notes:

[128] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 129.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group C v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[129] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.905 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.561 |
| upper limit | 1.46 |

Notes:

[129] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 130.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group C v Group H |
|-------------------|-------------------|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[130] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.273 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.798 |
| upper limit | 2.03 |

Notes:

[130] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 131.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group D v Group E |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[131] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 2.383 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.474 |
| upper limit | 3.851 |

Notes:

[131] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 132. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group D v Group F |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[132] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.202 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.754 |
| upper limit | 1.915 |

Notes:

[132] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 133.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group D v Group G |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[133] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.689 |
| upper limit | 1.821 |

Notes:

[133] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 134.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group D v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[134] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.576 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.987 |
| upper limit | 2.516 |

Notes:

[134] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 135.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group E v Group F |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[135] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.504 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.316 |
| upper limit | 0.805 |

Notes:

[135] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 136.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group E v Group G |
| Number of subjects included in analysis | 311 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[136] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.293 |
| upper limit | 0.754 |

Notes:

[136] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 137.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|-------------------|-------------------|
| Comparison groups | Group E v Group H |
|-------------------|-------------------|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[137] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.662 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.414 |
| upper limit | 1.056 |

Notes:

[137] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 138.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group F v Group G |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[138] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 0.932 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.583 |
| upper limit | 1.492 |

Notes:

[138] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|---|
| Statistical analysis title | 139.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|---|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group F v Group H |
| Number of subjects included in analysis | 310 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[139] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.312 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.831 |
| upper limit | 2.071 |

Notes:

[139] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 140. GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 387-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group G v Group H |
| Number of subjects included in analysis | 309 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[140] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 387 |
| Point estimate | 1.407 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.88 |
| upper limit | 2.249 |

Notes:

[140] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center

| | |
|-----------------------------------|--|
| Statistical analysis title | 25.GMT After Each Vaccination by Vaccine Group |
|-----------------------------------|--|

Statistical analysis description:

Day 22-For pairwise vaccine group compared, least squares GMT and associated 2-sided 95% CI, median, minimum, and maximum HI titer values were determined. The two-sided 95% CIs was calculated and assessed against a non-inferiority margin of 0.5. Subsequently the same non-inferiority hypothesis was tested using a non-inferiority margin of 0.67

| | |
|---|----------------------------------|
| Comparison groups | Group E v Group H |
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[141] |
| Method | ANOVA |
| Parameter estimate | Geometric Mean Ratio at day 22 |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.532 |
| upper limit | 1.203 |

Notes:

[141] - Log10-transformed HI antibody responses were modelled using analysis of variance (ANOVA) including factors for vaccine group and center.

Secondary: 3. Antibody Responses With and Without Seasonal Influenza Vaccination for Year 2009 to 2010

| | |
|---|---|
| End point title | 3. Antibody Responses With and Without Seasonal Influenza Vaccination for Year 2009 to 2010 |
| End point description: | |
| Subgroup analysis based on receipt of recent seasonal vaccination. Comparison between subjects previously vaccinated versus not vaccinated with seasonal influenza vaccines | |
| Subgroups without recent seasonal flu vaccine: | |
| PPS Day 1, Day 1-22 and Day 1-43 analysis set. N= 141, 147, 150, 148, 146, 146, 150, and 146 for Groups A, B, C, D, E, F, G, and H, respectively. | |
| PPS Day 1-29 analysis set. N= 132, 140, 143, 139, 138, 136, 139, and 138 for Groups A, B, C, D, E, F, G, and H, respectively. | |
| Subgroups with recent seasonal flu vaccine: | |
| PPS Day 1-22 and Day 1-43 analysis set. N= 11, 9, 6, 8, 9, 11, 6, and 7 for Groups A, B, C, D, E, F, G, and H, respectively | |
| PPS Day 1-29 analysis set. N= 11, 9, 6, 7, 9, 11, 5, and 6 for Groups A, B, C, D, E, F, G, and H, respectively. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 22, Day 29, Day 43 | |

| End point values | Group A | Group B | Group C | Group D |
|--|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 152 | 156 | 156 | 156 |
| Units: Percentages of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| Seroconversion (Day 22/Day 1)with seasonal flu vac | 73 (39 to 94) | 22 (3 to 60) | 83 (36 to 100) | 100 (63 to 100) |
| Seroconversion (Day 29/Day 1)with seasonal flu vac | 100 (72 to 100) | 67 (30 to 93) | 83 (36 to 100) | 100 (59 to 100) |
| Seroconversion (Day 43/Day 1)with seasonal flu vac | 91 (59 to 100) | 78 (40 to 97) | 67 (22 to 96) | 88 (47 to 100) |
| HI titer $\geq 1:40$ (Day 1)_ with seasonal flu vac | 18 (2 to 52) | 22 (3 to 60) | 50 (12 to 88) | 38 (9 to 76) |
| HI titer $\geq 1:40$ (Day 22)_ with seasonal flu vac | 73 (39 to 94) | 33 (7 to 70) | 100 (54 to 100) | 100 (63 to 100) |
| HI titer $\geq 1:40$ (Day 29)_ with seasonal flu vac | 100 (72 to 100) | 67 (30 to 93) | 100 (54 to 100) | 100 (59 to 100) |
| HI titer $\geq 1:40$ (Day 43)_ with seasonal flu vac | 100 (72 to 100) | 78 (40 to 97) | 100 (54 to 100) | 100 (63 to 100) |
| Seroconversion (Day 22/Day 1)without flu vac | 82 (75 to 88) | 47 (39 to 55) | 77 (70 to 84) | 88 (81 to 93) |
| Seroconversion (Day 29/Day 1)without flu vac | 98 (95 to 100) | 79 (71 to 85) | 99 (96 to 100) | 99 (95 to 100) |
| Seroconversion (Day 43/Day 1)without flu vac | 99 (95 to 100) | 78 (70 to 84) | 98 (94 to 100) | 98 (94 to 100) |
| HI titer $\geq 1:40$ (Day 1) without flu vac | 10 (6 to 16) | 8 (4 to 14) | 11 (7 to 18) | 9 (5 to 15) |
| HI titer $\geq 1:40$ (Day 22)without flu vac | 84 (77 to 90) | 49 (41 to 57) | 80 (73 to 86) | 91 (85 to 95) |
| HI titer $\geq 1:40$ (Day 29) without flu vac | 99 (96 to 100) | 79 (72 to 86) | 100 (97 to 100) | 99 (95 to 100) |
| HI titer $\geq 1:40$ (Day 43) without flu vac | 99 (96 to 100) | 79 (71 to 85) | 100 (98 to 100) | 99 (95 to 100) |

| End point values | Group E | Group F | Group G | Group H |
|------------------|---------|---------|---------|---------|
|------------------|---------|---------|---------|---------|

| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
|--|-----------------|-----------------|-----------------|-----------------|
| Number of subjects analysed | 155 | 157 | 156 | 153 |
| Units: Percentages of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| Seroconversion (Day 22/Day 1)with seasonal flu vac | 44 (14 to 79) | 73 (39 to 94) | 100 (54 to 100) | 71 (29 to 96) |
| Seroconversion (Day 29/Day 1)with seasonal flu vac | 67 (30 to 93) | 100 (72 to 100) | 100 (48 to 100) | 83 (36 to 100) |
| Seroconversion (Day 43/Day 1)with seasonal flu vac | 78 (40 to 97) | 100 (72 to 100) | 100 (54 to 100) | 86 (42 to 100) |
| HI titer $\geq 1:40$ (Day 1)_ with seasonal flu vac | 0 (0 to 34) | 9 (0 to 41) | 17 (0 to 64) | 0 (0 to 41) |
| HI titer $\geq 1:40$ (Day 22)_ with seasonal flu vac | 44 (14 to 79) | 73 (39 to 94) | 100 (54 to 100) | 71 (29 to 96) |
| HI titer $\geq 1:40$ (Day 29)_ with seasonal flu vac | 67 (30 to 93) | 100 (72 to 100) | 100 (48 to 100) | 100 (54 to 100) |
| HI titer $\geq 1:40$ (Day 43)_ with seasonal flu vac | 78 (40 to 97) | 100 (72 to 100) | 100 (54 to 100) | 86 (42 to 100) |
| Seroconversion (Day 22/Day 1)without flu vac | 59 (50 to 67) | 82 (75 to 88) | 91 (86 to 95) | 60 (51 to 68) |
| Seroconversion (Day 29/Day 1)without flu vac | 88 (82 to 93) | 100 (97 to 100) | 100 (97 to 100) | 94 (89 to 97) |
| Seroconversion (Day 43/Day 1)without flu vac | 85 (78 to 90) | 99 (95 to 100) | 99 (96 to 100) | 88 (82 to 93) |
| HI titer $\geq 1:40$ (Day 1) without flu vac | 16 (11 to 23) | 9 (5 to 15) | 7 (4 to 13) | 13 (8 to 20) |
| HI titer $\geq 1:40$ (Day 22)without flu vac | 62 (53 to 70) | 83 (76 to 89) | 93 (88 to 97) | 65 (57 to 73) |
| HI titer $\geq 1:40$ (Day 29) without flu vac | 90 (84 to 94) | 100 (97 to 100) | 100 (97 to 100) | 96 (92 to 99) |
| HI titer $\geq 1:40$ (Day 43) without flu vac | 88 (81 to 93) | 99 (96 to 100) | 100 (98 to 100) | 92 (86 to 96) |

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Geometric Mean Titers (GMTs) With and Without Seasonal Influenza Vaccination for Year 2009 to 2010

| | |
|-----------------|---|
| End point title | 4. Geometric Mean Titers (GMTs) With and Without Seasonal Influenza Vaccination for Year 2009 to 2010 |
|-----------------|---|

End point description:

Subgroup analysis based on receipt of recent seasonal vaccination. Comparison between subjects previously vaccinated versus not vaccinated with seasonal influenza vaccines

Subgroups without recent seasonal flu vaccine:

PPS Day 1, Day 1–22 and Day 1–43 analysis set. N= 141, 147, 150, 148, 146, 146, 150, and 146 for Groups A, B, C, D, E, F, G, and H, respectively.

PPS Day 1–29 analysis set. N= 132, 140, 143, 139, 138, 136, 139, and 138 for Groups A, B, C, D, E, F, G, and H, respectively.

Subgroups with recent seasonal flu vaccine:

PPS Day 1–22 and Day 1–43 analysis set. N= 11, 9, 6, 8, 9, 11, 6, and 7 for Groups A, B, C, D, E, F, G, and H, respectively

PPS Day 1–29 analysis set. N= 11, 9, 6, 7, 9, 11, 5, and 6 for Groups A, B, C, D, E, F, G, and H, respectively.

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

End point timeframe:

Day 1, Day 22, Day 29, Day 43

| End point values | Group A | Group B | Group C | Group D |
|--|-------------------|---------------------|-------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 152 | 156 | 156 | 156 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 1_ with seasonal flu vaccination | 6.22 (2.16 to 18) | 12 (3.63 to 42) | 22 (5.54 to 90) | 15 (4.5 to 47) |
| Day 22_ with seasonal flu vaccination | 36 (9.11 to 146) | 44 (8.93 to 217) | 196 (32 to 1213) | 209 (45 to 976) |
| Day 29_ with seasonal flu vaccination | 278 (90 to 856) | 171 (47 to 625) | 785 (178 to 3450) | 1186 (317 to 4440) |
| Day 43_ with seasonal flu vaccination | 260 (102 to 665) | 182 (62 to 537) | 503 (146 to 1729) | 594 (209 to 1687) |
| Day 1_ without seasonal flu vaccination | 8.54 (7.03 to 10) | 7.08 (5.84 to 8.59) | 8.3 (6.86 to 10) | 7.76 (6.41 to 9.41) |
| Day 22_ without seasonal flu vaccination | 115 (83 to 161) | 28 (20 to 38) | 85 (61 to 117) | 159 (115 to 220) |
| Day 29_ without seasonal flu vaccination | 810 (633 to 1037) | 144 (113 to 183) | 669 (527 to 849) | 968 (760 to 1232) |
| Day 43_ without seasonal flu vaccination | 600 (477 to 753) | 115 (92 to 144) | 477 (381 to 596) | 643 (514 to 805) |

| End point values | Group E | Group F | Group G | Group H |
|--|-------------------|---------------------|--------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 155 | 157 | 156 | 153 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 1_ with seasonal flu vaccination | 5.42 (1.75 to 17) | 5.99 (2.16 to 17) | 15 (3.94 to 565) | 9.36 (2.69 to 33) |
| Day 22_ with seasonal flu vaccination | 48 (11 to 210) | 44 (11 to 166) | 345 (61 to 1961) | 111 (22 to 567) |
| Day 29_ with seasonal flu vaccination | 137 (41 to 457) | 670 (226 to 1988) | 771 (164 to 3628) | 184 (43 to 791) |
| Day 43_ with seasonal flu vaccination | 81 (30 to 221) | 663 (268 to 1639) | 1035 (319 to 3363) | 228 (75 to 689) |
| Day 1_ without seasonal flu vaccination | 9.35 (7.71 to 11) | 7.47 (6.15 to 9.08) | 6.8 (5.61 to 8.24) | 9.1 (7.51 to 11) |
| Day 22_ without seasonal flu vaccination | 52 (38 to 72) | 109 (79 to 152) | 158 (114 to 218) | 62 (45 to 85) |
| Day 29_ without seasonal flu vaccination | 228 (179 to 291) | 756 (591 to 966) | 1080 (847 to 1377) | 297 (233 to 377) |
| Day 43_ without seasonal flu vaccination | 182 (145 to 228) | 520 (414 to 653) | 770 (615 to 963) | 224 (179 to 281) |

Statistical analyses

Secondary: 5. Antibody Response Based on Baseline Seropositivity

| | |
|--|---|
| End point title | 5. Antibody Response Based on Baseline Seropositivity |
| End point description: | |
| Subgroup analysis based on Subjects with a pre-vaccination HI antibody titer < 1:10 and pre-vaccination HI antibody titer ≥ 1:10 | |
| Subgroups with baseline HI titer < 1:10: PPS Day 1–29 analysis set. N= 104, 116, 111, 107, 109, 113, 120, and 103 for Groups A, B, C, D, E, F, G, and H, respectively. | |
| Subgroups with baseline HI titer ≥ 1:10: PPS Day 1–29 analysis set. N= 39, 33, 38, 39, 38, 34, 24, and 41 for Groups A, B, C, D, E, F, G, and H, respectively | |
| End point type | Secondary |
| End point timeframe: | |
| Day 22, Day 29, Day 43 | |

| End point values | Group A | Group B | Group C | Group D |
|---|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 152 | 156 | 156 | 156 |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Seroconversion (Day 22/Day 1)_ baseline HI < 1:10 | 81 (72 to 88) | 39 (30 to 48) | 79 (71 to 86) | 90 (84 to 95) |
| Seroconversion (Day 29/Day 1)_ baseline HI < 1:10 | 99 (95 to 100) | 75 (66 to 83) | 100 (97 to 100) | 98 (93 to 100) |
| Seroconversion (Day 43/Day 1)_ baseline HI < 1:10 | 99 (95 to 100) | 75 (67 to 83) | 100 (97 to 100) | 98 (94 to 100) |
| HI titer ≥1:40 (Day 1)_ baseline HI < 1:10 | 0 (0 to 3) | 0 (0 to 3) | 0 (0 to 3) | 0 (0 to 3) |
| HI titer ≥1:40 (Day 22)_ baseline HI < 1:10 | 81 (72 to 88) | 39 (30 to 48) | 79 (71 to 86) | 90 (84 to 95) |
| HI titer ≥1:40 (Day 29)_ baseline HI < 1:10 | 99 (95 to 100) | 75 (66 to 83) | 100 (97 to 100) | 98 (93 to 100) |
| HI titer ≥1:40 (Day 43)_ baseline HI < 1:10 | 99 (95 to 100) | 75 (67 to 83) | 100 (97 to 100) | 98 (94 to 100) |
| Seroconversion (Day 22/Day 1)_ baseline HI ≥ 1:10 | 83 (69 to 93) | 69 (51 to 83) | 73 (57 to 86) | 83 (68 to 93) |
| Seroconversion (Day 29/Day 1)_ baseline HI ≥ 1:10 | 97 (87 to 100) | 88 (72 to 97) | 95 (82 to 99) | 100 (91 to 100) |
| Seroconversion (Day 43/Day 1)_ baseline HI ≥ 1:10 | 95 (84 to 99) | 86 (70 to 95) | 88 (74 to 96) | 95 (83 to 99) |
| HI titer ≥1:40 (Day 1)_ baseline HI ≥ 1:10 | 38 (24 to 54) | 40 (24 to 58) | 49 (33 to 65) | 41 (26 to 58) |
| HI titer ≥1:40 (Day 22)_ baseline HI ≥ 1:10 | 90 (77 to 97) | 80 (63 to 92) | 85 (71 to 94) | 93 (80 to 98) |
| HI titer ≥1:40 (Day 29)_ baseline HI ≥ 1:10 | 100 (91 to 100) | 91 (76 to 98) | 100 (91 to 100) | 100 (91 to 100) |
| HI titer ≥1:40 (Day 43)_ baseline HI ≥ 1:10 | 100 (92 to 100) | 91 (77 to 98) | 100 (91 to 100) | 100 (91 to 100) |

| End point values | Group E | Group F | Group G | Group H |
|------------------|---------|---------|---------|---------|
|------------------|---------|---------|---------|---------|

| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
|---|-----------------|-----------------|-----------------|-----------------|
| Number of subjects analysed | 155 | 157 | 156 | 153 |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Seroconversion (Day 22/Day 1)_ baseline HI < 1:10 | 54 (44 to 63) | 78 (69 to 85) | 92 (86 to 96) | 61 (52 to 70) |
| Seroconversion (Day 29/Day 1)_ baseline HI < 1:10 | 85 (77 to 91) | 100 (97 to 100) | 100 (97 to 100) | 97 (92 to 99) |
| Seroconversion (Day 43/Day 1)_ baseline HI < 1:10 | 83 (75 to 90) | 99 (95 to 100) | 100 (97 to 100) | 91 (84 to 96) |
| HI titer ≥1:40 (Day 1)_ baseline HI < 1:10 | 0 (0 to 3) | 0 (0 to 3) | 0 (0 to 3) | 0 (0 to 3) |
| HI titer ≥1:40 (Day 22)_ baseline HI < 1:10 | 54 (44 to 63) | 78 (69 to 85) | 92 (86 to 96) | 61 (52 to 70) |
| HI titer ≥1:40 (Day 29)_ baseline HI < 1:10 | 85 (77 to 91) | 100 (97 to 100) | 100 (97 to 100) | 97 (92 to 99) |
| HI titer ≥1:40 (Day 43)_ baseline HI < 1:10 | 83 (75 to 90) | 99 (95 to 100) | 100 (97 to 100) | 91 (84 to 96) |
| Seroconversion (Day 22/Day 1)_ baseline HI ≥ 1:10 | 71 (54 to 84) | 95 (82 to 99) | 89 (72 to 98) | 57 (41 to 72) |
| Seroconversion (Day 29/Day 1)_ baseline HI ≥ 1:10 | 92 (79 to 98) | 100 (90 to 100) | 100 (86 to 100) | 85 (71 to 94) |
| Seroconversion (Day 43/Day 1)_ baseline HI ≥ 1:10 | 88 (74 to 96) | 97 (86 to 100) | 96 (82 to 100) | 81 (66 to 91) |
| HI titer ≥1:40 (Day 1)_ baseline HI ≥ 1:10 | 59 (42 to 74) | 38 (22 to 55) | 43 (24 to 63) | 45 (30 to 61) |
| HI titer ≥1:40 (Day 22)_ baseline HI ≥ 1:10 | 80 (65 to 91) | 97 (86 to 100) | 100 (88 to 100) | 76 (61 to 88) |
| HI titer ≥1:40 (Day 29)_ baseline HI ≥ 1:10 | 97 (86 to 100) | 100 (90 to 100) | 100 (86 to 100) | 95 (83 to 99) |
| HI titer ≥1:40 (Day 43)_ baseline HI ≥ 1:10 | 98 (87 to 100) | 100 (91 to 100) | 100 (88 to 100) | 93 (81 to 99) |

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Geometric Mean Titers (GMTs) Based on Baseline Seropositivity

| | |
|-----------------|--|
| End point title | 6. Geometric Mean Titers (GMTs) Based on Baseline Seropositivity |
|-----------------|--|

End point description:

Subgroup analysis based on Subjects with a pre-vaccination HI antibody titer < 1:10 and pre-vaccination HI antibody titer ≥ 1:10

Immunogenicity responses in subjects who are seropositive (A/H1N1 2009 HI titer ≥ 1:10) at Baseline (Day 1 (pre-vaccination)) as compared to those who are seronegative (HI titer < 1:10)

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

End point timeframe:

Day 1, Day 22, Day 29, Day 43.

| End point values | Group A | Group B | Group C | Group D |
|---|--------------------|------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 152 | 156 | 156 | 156 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| GMTDay 1 HI < 1:10(110,121,115,115,114,120,128,11 | 5 (5 to 5.1) | 5 (5 to 5.1) | 5.1 (5 to 5.1) | 5.1 (5 to 5.1) |
| GMTDay 22 HI< 1:10(110,121,115,115,114,120,128,11 | 80 (57 to 111) | 18 (13 to 25) | 62 (45 to 85) | 130 (94 to 180) |
| GMTDay 29HI < 1:10(110,121,115,115,114,120,128,11 | 664 (505 to 872) | 100 (78 to 130) | 638 (490 to 830) | 885 (676 to 1157) |
| GMTDay 43HI < 1:10(110,121,115,115,114,120,128,11 | 490 (381 to 630) | 85 (67 to 108) | 437 (342 to 559) | 568 (444 to 727) |
| GMT Day 1 HI ≥ 1:10 (42,35,41,41,41,37,28,42) | 40 (28 to 57) | 32 (21 to 47) | 47 (32 to 68) | 32 (22 to 46) |
| GMT Day 22_HI ≥ 1:10(42,35,41,41,41,37,28,42) | 343 (187 to 628) | 132 (68 to 258) | 311 (164 to 590) | 320 (171 to 599) |
| GMT Day 29_HI ≥ 1:10(42,35,41,41,41,37,28,42) | 1178 (782 to 1776) | 460 (294 to 721) | 1063 (689 to 1640) | 1281 (843 to 1948) |
| GMT Day 43_HI ≥ 1:10(42,35,41,41,41,37,28,42) | 876 (604 to 1271) | 320 (212 to 482) | 657 (443 to 974) | 881 (599 to 1295) |

| End point values | Group E | Group F | Group G | Group H |
|---|------------------|--------------------|---------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 155 | 157 | 156 | 153 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| GMTDay 1 HI < 1:10(110,121,115,115,114,120,128,11 | 5 (5 to 5.1) | 5 (5 to 5.07) | 5.1 (5 to 5.2) | 5.1 (5 to 5.2) |
| GMTDay 22 HI< 1:10(110,121,115,115,114,120,128,11 | 26 (19 to 36) | 72 (52 to 98) | 130 (96 to 177) | 39 (28 to 54) |
| GMTDay 29HI < 1:10(110,121,115,115,114,120,128,11 | 149 (114 to 194) | 685 (527 to 890) | 950 (736 to 1227) | 234 (179 to 307) |
| GMTDay 43HI < 1:10(110,121,115,115,114,120,128,11 | 121 (95 to 155) | 463 (363 to 590) | 717 (566 to 908) | 177 (138 to 227) |
| GMT Day 1 HI ≥ 1:10 (42,35,41,41,41,37,28,42) | 52 (36 to 75) | 35 (24 to 52) | 40 (26 to 63) | 48 (33 to 69) |
| GMT Day 22_HI ≥ 1:10(42,35,41,41,41,37,28,42) | 284 (151 to 532) | 417 (217 to 802) | 460 (219 to 965) | 252 (134 to 475) |
| GMT Day 29_HI ≥ 1:10(42,35,41,41,41,37,28,42) | 543 (356 to 830) | 1197 (771 to 1857) | 2088 (1240 to 3516) | 641 (422 to 973) |
| GMT Day 43_HI ≥ 1:10(42,35,41,41,41,37,28,42) | 464 (316 to 684) | 838 (561 to 1253) | 1184 (751 to 1867) | 428 (290 to 631) |

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Number of Participants Reporting Solicited Local and Systemic Reactions After First Vaccination

| | |
|---|--|
| End point title | 7. Number of Participants Reporting Solicited Local and Systemic Reactions After First Vaccination |
| End point description: | |
| Safety was measured in terms of the Number of Participants Reporting Solicited Local and Systemic Reactions After First Vaccination | |
| End point type | Secondary |
| End point timeframe: | |
| Days 1 to 7 | |

| End point values | Group A | Group B | Group C | Group D |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 171 | 167 | 167 | 168 |
| Units: Number of subjects | | | | |
| Pain | 62 | 43 | 52 | 86 |
| Erythema | 3 | 2 | 4 | 3 |
| Swelling | 8 | 5 | 5 | 7 |
| Induration | 14 | 5 | 10 | 12 |
| Tenderness | 72 | 49 | 59 | 96 |
| Chills | 8 | 3 | 9 | 11 |
| Myalgia | 16 | 8 | 13 | 27 |
| Arthralgia | 7 | 3 | 9 | 7 |
| Headache | 24 | 15 | 30 | 37 |
| Nausea | 10 | 14 | 13 | 14 |
| Vomiting | 4 | 5 | 10 | 4 |
| Diarrhea | 12 | 7 | 6 | 2 |
| Fatigue | 27 | 17 | 23 | 29 |
| Fever | 9 | 10 | 13 | 14 |
| Stayed home | 1 | 0 | 0 | 0 |
| Analg./antip.used | 1 | 0 | 0 | 0 |

| End point values | Group E | Group F | Group G | Group H |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 167 | 168 | 166 | 165 |
| Units: Number of subjects | | | | |
| Pain | 47 | 65 | 72 | 51 |
| Erythema | 1 | 1 | 6 | 5 |
| Swelling | 11 | 11 | 10 | 6 |
| Induration | 10 | 11 | 15 | 12 |
| Tenderness | 50 | 78 | 69 | 60 |
| Chills | 5 | 8 | 8 | 8 |
| Myalgia | 8 | 15 | 17 | 12 |
| Arthralgia | 3 | 8 | 7 | 3 |
| Headache | 16 | 25 | 27 | 17 |
| Nausea | 7 | 11 | 12 | 9 |
| Vomiting | 5 | 8 | 5 | 5 |
| Diarrhea | 10 | 3 | 4 | 6 |

| | | | | |
|-------------------|----|----|----|----|
| Fatigue | 17 | 23 | 29 | 16 |
| Fever | 9 | 17 | 16 | 7 |
| Stayed home | 0 | 1 | 1 | 0 |
| Analg./antip.used | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Number of Participants Reporting Solicited Local and Systemic Reactions After Second Vaccination

| | |
|-----------------|---|
| End point title | 8. Number of Participants Reporting Solicited Local and Systemic Reactions After Second Vaccination |
|-----------------|---|

End point description:

Safety was measured in terms of the Number of Participants Reporting Solicited Local and Systemic Reactions After Second Vaccination

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

End point timeframe:

Day 22 to 28

| End point values | Group A | Group B | Group C | Group D |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 165 | 163 | 164 | 163 |
| Units: Number of subjects | | | | |
| Pain | 53 | 35 | 46 | 59 |
| Erythema | 3 | 1 | 4 | 4 |
| Swelling | 8 | 5 | 10 | 9 |
| Induration | 10 | 2 | 9 | 6 |
| Tenderness | 55 | 42 | 50 | 65 |
| Chills | 7 | 5 | 5 | 4 |
| Myalgia | 12 | 4 | 9 | 16 |
| Arthralgia | 2 | 0 | 1 | 4 |
| Headache | 12 | 12 | 12 | 19 |
| Nausea | 11 | 7 | 5 | 6 |
| Vomiting | 6 | 3 | 4 | 7 |
| Diarrhea | 6 | 6 | 5 | 5 |
| Fatigue | 16 | 11 | 15 | 14 |
| Fever | 10 | 6 | 5 | 5 |
| Stayed home | 1 | 0 | 0 | 0 |
| Analg./antip.used | 0 | 0 | 0 | 0 |

| End point values | Group E | Group F | Group G | Group H |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 162 | 167 | 162 | 164 |

| Units: Number of subjects | | | | |
|---------------------------|----|----|----|----|
| Pain | 42 | 57 | 48 | 50 |
| Erythema | 5 | 4 | 5 | 5 |
| Swelling | 11 | 10 | 12 | 10 |
| Induration | 9 | 15 | 13 | 10 |
| Tenderness | 38 | 67 | 57 | 54 |
| Chills | 7 | 4 | 3 | 3 |
| Myalgia | 6 | 8 | 9 | 15 |
| Arthralgia | 2 | 2 | 0 | 2 |
| Headache | 14 | 11 | 13 | 9 |
| Nausea | 8 | 16 | 4 | 5 |
| Vomiting | 3 | 3 | 3 | 3 |
| Diarrhea | 7 | 7 | 2 | 4 |
| Fatigue | 17 | 10 | 13 | 6 |
| Fever | 10 | 8 | 7 | 4 |
| Stayed home | 1 | 0 | 0 | 0 |
| Analg./antip.used | 0 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of Participants Reporting Unsolicited Adverse Events(AEs)

| | |
|-----------------|---|
| End point title | 9. Number of Participants Reporting Unsolicited Adverse Events(AEs) |
|-----------------|---|

End point description:

Safety was measured in terms of the Number of Participants Reporting Unsolicited AEs

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

End point timeframe:

Safety monitoring periods were the Primary Period: Day 1 (1st vaccination) through ≤21 days post second vaccination, and the Follow-up Period: >21 Days post second vaccination to 12 months after second vaccination

| End point values | Group A | Group B | Group C | Group D |
|--|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 171 | 168 | 169 | 168 |
| Units: Number of Subjects | | | | |
| AEs: all (Days 1–43) | 98 | 80 | 80 | 85 |
| SAEs: all (Days 1–43) | 0 | 0 | 1 | 0 |
| AEs leading to premature withdrawal (Days 1–43) | 0 | 0 | 1 | 0 |
| AEs leading to new onset of chronic disorder | 0 | 0 | 0 | 0 |
| AE leading to medically attended visits(Days 1–43) | 31 | 34 | 25 | 40 |
| AEs: all (Days 44–387) | 95 | 98 | 102 | 93 |
| SAEs: all (Days 44–387) | 0 | 5 | 6 | 4 |

| | | | | |
|--|----|----|-----|----|
| AEs leading to premature withdrawal (Days 44–387) | 0 | 0 | 1 | 0 |
| AEs leading to new onset of chronic dis. | 2 | 7 | 4 | 3 |
| AE leading to medically attended visit(Days44–387) | 95 | 97 | 102 | 93 |

| End point values | Group E | Group F | Group G | Group H |
|--|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 168 | 168 | 167 | 169 |
| Units: Number of Subjects | | | | |
| AEs: all (Days 1–43) | 86 | 93 | 79 | 79 |
| SAEs: all (Days 1–43) | 0 | 0 | 0 | 0 |
| AEs leading to premature withdrawal (Days 1–43) | 0 | 0 | 0 | 0 |
| AEs leading to new onset of chronic disorder | 0 | 1 | 0 | 0 |
| AE leading to medically attended visits(Days 1–43) | 34 | 35 | 28 | 24 |
| AEs: all (Days 44–387) | 90 | 101 | 90 | 95 |
| SAEs: all (Days 44–387) | 3 | 4 | 1 | 0 |
| AEs leading to premature withdrawal (Days 44–387) | 0 | 0 | 0 | 0 |
| AEs leading to new onset of chronic dis. | 4 | 3 | 6 | 3 |
| AE leading to medically attended visit(Days44–387) | 90 | 100 | 89 | 95 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through Day 387

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Group A |
|-----------------------|---------|

Reporting group description:

3.75_(50) MF59-[3.75 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22]

| | |
|-----------------------|---------|
| Reporting group title | Group B |
|-----------------------|---------|

Reporting group description:

7.5_(0) MF59-[7.5 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22]

| | |
|-----------------------|---------|
| Reporting group title | Group C |
|-----------------------|---------|

Reporting group description:

7.5_(50) MF59-[7.5 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22]

| | |
|-----------------------|---------|
| Reporting group title | Group D |
|-----------------------|---------|

Reporting group description:

7.5_(100) MF59-[7.5 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22]

| | |
|-----------------------|---------|
| Reporting group title | Group E |
|-----------------------|---------|

Reporting group description:

15_(0) MF59-[15 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22]

| | |
|-----------------------|---------|
| Reporting group title | Group F |
|-----------------------|---------|

Reporting group description:

15_(50) MF59-[15 µg A/H1N1 antigen with 50% MF59 adjuvant administered on study day 1 and day 22]

| | |
|-----------------------|---------|
| Reporting group title | Group G |
|-----------------------|---------|

Reporting group description:

15_(100) MF59-[15 µg A/H1N1 antigen with 100% MF59 adjuvant administered on study day 1 and day 22]

| | |
|-----------------------|---------|
| Reporting group title | Group H |
|-----------------------|---------|

Reporting group description:

30_(0) MF59-[30 µg A/H1N1 antigen without MF59 adjuvant administered on study day 1 and day 22]

| Serious adverse events | Group A | Group B | Group C |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 5 / 168 (2.98%) | 7 / 169 (4.14%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Fall | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign Body | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna Fracture | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 1 / 169 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 168 (0.60%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 1 / 169 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Cerumen Impaction | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 168 (0.60%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian Mass | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngeal stenosis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumomediastinum | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 168 (0.60%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Swelling Face | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bipolar Disorder | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Intermittent explosive disorder subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oppositional defiant disorder subjects affected / exposed | 0 / 171 (0.00%) | 1 / 168 (0.60%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post-traumatic Stress Disorder subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 1 / 169 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis perforated subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 1 / 169 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic Tonsillitis subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonsillar abscess subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 1 / 169 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis Streptococcal subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pharyngotonsillitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 168 (0.60%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 1 / 169 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal scalded skin syndrome | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral Infection | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 0 / 169 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 168 (0.00%) | 1 / 169 (0.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Group D | Group E | Group F |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 168 (2.38%) | 3 / 168 (1.79%) | 4 / 168 (2.38%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 1 / 168 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign Body | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 168 (0.00%) | 1 / 168 (0.60%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna Fracture | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 1 / 168 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Cerumen Impaction | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian Mass | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 1 / 168 (0.60%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 1 / 168 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngeal stenosis | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 1 / 168 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumomediastinum | | | |
| subjects affected / exposed | 1 / 168 (0.60%) | 0 / 168 (0.00%) | 0 / 168 (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 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Swelling Face | | | |
| subjects affected / exposed | 1 / 168 (0.60%) | 0 / 168 (0.00%) | 0 / 168 (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 |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 1 / 168 (0.60%) | 0 / 168 (0.00%) | 0 / 168 (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 |
| Bipolar Disorder | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intermittent explosive disorder | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oppositional defiant disorder | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post-traumatic Stress Disorder | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic Tonsillitis | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 1 / 168 (0.60%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 1 / 168 (0.60%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis Streptococcal | | | |
| subjects affected / exposed | 1 / 168 (0.60%) | 0 / 168 (0.00%) | 0 / 168 (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 |
| pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 0 / 168 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 168 (0.60%) | 0 / 168 (0.00%) | 0 / 168 (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 |
| Staphylococcal scalded skin syndrome | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 1 / 168 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral Infection | | | |
| subjects affected / exposed | 1 / 168 (0.60%) | 0 / 168 (0.00%) | 0 / 168 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 168 (0.00%) | 1 / 168 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Group G | Group H | |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign Body | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulna Fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Cerumen Impaction | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Ovarian Mass | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngeal stenosis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumomediastinum | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wheezing | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Swelling Face | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bipolar Disorder | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intermittent explosive disorder | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oppositional defiant disorder | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post-traumatic Stress Disorder | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Tonsillitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis Streptococcal | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal scalded skin syndrome | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral Infection | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 0 / 169 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Group A | Group B | Group C |
|---|--------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 148 / 171 (86.55%) | 125 / 168 (74.40%) | 141 / 169 (83.43%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 37 / 171 (21.64%) | 31 / 168 (18.45%) | 41 / 169 (24.26%) |
| occurrences (all) | 51 | 44 | 49 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 17 / 171 (9.94%) | 8 / 168 (4.76%) | 14 / 169 (8.28%) |
| occurrences (all) | 17 | 8 | 16 |
| Fatigue | | | |
| subjects affected / exposed | 35 / 171 (20.47%) | 24 / 168 (14.29%) | 31 / 169 (18.34%) |
| occurrences (all) | 48 | 32 | 43 |
| Injection site erythema | | | |
| subjects affected / exposed | 7 / 171 (4.09%) | 3 / 168 (1.79%) | 7 / 169 (4.14%) |
| occurrences (all) | 7 | 3 | 8 |
| Injection site induration | | | |
| subjects affected / exposed | 6 / 171 (3.51%) | 0 / 168 (0.00%) | 4 / 169 (2.37%) |
| occurrences (all) | 6 | 0 | 5 |

| | | | |
|---|---------------------------|--------------------------|--------------------------|
| Injection site Pain subjects affected / exposed occurrences (all) | 102 / 171 (59.65%) 251 | 73 / 168 (43.45%) 178 | 86 / 169 (50.89%) 212 |
| Injection site swelling subjects affected / exposed occurrences (all) | 7 / 171 (4.09%) 8 | 4 / 168 (2.38%) 4 | 8 / 169 (4.73%) 10 |
| Pyrexia subjects affected / exposed occurrences (all) | 41 / 171 (23.98%) 49 | 34 / 168 (20.24%) 42 | 38 / 169 (22.49%) 47 |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 22 / 171 (12.87%) 28 | 16 / 168 (9.52%) 19 | 17 / 169 (10.06%) 21 |
| Nausea subjects affected / exposed occurrences (all) | 21 / 171 (12.28%) 30 | 22 / 168 (13.10%) 26 | 14 / 169 (8.28%) 20 |
| Vomiting subjects affected / exposed occurrences (all) | 22 / 171 (12.87%) 23 | 14 / 168 (8.33%) 19 | 27 / 169 (15.98%) 32 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma subjects affected / exposed occurrences (all) | 14 / 171 (8.19%) 21 | 8 / 168 (4.76%) 13 | 10 / 169 (5.92%) 13 |
| Cough subjects affected / exposed occurrences (all) | 34 / 171 (19.88%) 50 | 35 / 168 (20.83%) 43 | 30 / 169 (17.75%) 34 |
| Nasal Congestion subjects affected / exposed occurrences (all) | 12 / 171 (7.02%) 12 | 7 / 168 (4.17%) 8 | 6 / 169 (3.55%) 6 |
| Oropharyngeal Pain subjects affected / exposed occurrences (all) | 13 / 171 (7.60%) 14 | 9 / 168 (5.36%) 10 | 5 / 169 (2.96%) 5 |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 8 / 171 (4.68%) 8 | 11 / 168 (6.55%) 11 | 6 / 169 (3.55%) 6 |
| Rhinorrhoea | | | |

| | | | |
|--|------------------------|-----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 10 / 171 (5.85%) 15 | 9 / 168 (5.36%) 11 | 7 / 169 (4.14%) 7 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 9 / 171 (5.26%) | 3 / 168 (1.79%) | 13 / 169 (7.69%) |
| occurrences (all) | 10 | 3 | 14 |
| Myalgia | | | |
| subjects affected / exposed | 24 / 171 (14.04%) | 11 / 168 (6.55%) | 18 / 169 (10.65%) |
| occurrences (all) | 30 | 12 | 25 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 13 / 171 (7.60%) | 8 / 168 (4.76%) | 5 / 169 (2.96%) |
| occurrences (all) | 14 | 8 | 5 |
| Conjunctivitis | | | |
| subjects affected / exposed | 3 / 171 (1.75%) | 8 / 168 (4.76%) | 6 / 169 (3.55%) |
| occurrences (all) | 3 | 8 | 6 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 14 / 171 (8.19%) | 4 / 168 (2.38%) | 10 / 169 (5.92%) |
| occurrences (all) | 14 | 5 | 10 |
| Otitis Media | | | |
| subjects affected / exposed | 17 / 171 (9.94%) | 14 / 168 (8.33%) | 28 / 169 (16.57%) |
| occurrences (all) | 21 | 16 | 37 |
| Otitis Media acute | | | |
| subjects affected / exposed | 9 / 171 (5.26%) | 3 / 168 (1.79%) | 4 / 169 (2.37%) |
| occurrences (all) | 10 | 3 | 4 |
| Pharyngitis | | | |
| subjects affected / exposed | 13 / 171 (7.60%) | 9 / 168 (5.36%) | 14 / 169 (8.28%) |
| occurrences (all) | 16 | 11 | 20 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 17 / 171 (9.94%) | 19 / 168 (11.31%) | 18 / 169 (10.65%) |
| occurrences (all) | 28 | 24 | 23 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 29 / 171 (16.96%) | 36 / 168 (21.43%) | 23 / 169 (13.61%) |
| occurrences (all) | 40 | 46 | 28 |
| Viral Infection | | | |

| | | | |
|-----------------------------|------------------|-----------------|------------------|
| subjects affected / exposed | 13 / 171 (7.60%) | 5 / 168 (2.98%) | 11 / 169 (6.51%) |
| occurrences (all) | 13 | 5 | 12 |
| Sinusitis | | | |
| subjects affected / exposed | 9 / 171 (5.26%) | 7 / 168 (4.17%) | 7 / 169 (4.14%) |
| occurrences (all) | 11 | 8 | 8 |

| Non-serious adverse events | Group D | Group E | Group F |
|---|--------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 152 / 168 (90.48%) | 139 / 168 (82.74%) | 146 / 168 (86.90%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 46 / 168 (27.38%) | 29 / 168 (17.26%) | 38 / 168 (22.62%) |
| occurrences (all) | 72 | 38 | 52 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 14 / 168 (8.33%) | 12 / 168 (7.14%) | 12 / 168 (7.14%) |
| occurrences (all) | 15 | 12 | 12 |
| Fatigue | | | |
| subjects affected / exposed | 34 / 168 (20.24%) | 30 / 168 (17.86%) | 31 / 168 (18.45%) |
| occurrences (all) | 47 | 36 | 41 |
| Injection site erythema | | | |
| subjects affected / exposed | 8 / 168 (4.76%) | 8 / 168 (4.76%) | 7 / 168 (4.17%) |
| occurrences (all) | 8 | 9 | 8 |
| Injection site induration | | | |
| subjects affected / exposed | 5 / 168 (2.98%) | 4 / 168 (2.38%) | 5 / 168 (2.98%) |
| occurrences (all) | 6 | 4 | 5 |
| Injection site Pain | | | |
| subjects affected / exposed | 119 / 168 (70.83%) | 86 / 168 (51.19%) | 100 / 168 (59.52%) |
| occurrences (all) | 316 | 185 | 271 |
| Injection site swelling | | | |
| subjects affected / exposed | 8 / 168 (4.76%) | 10 / 168 (5.95%) | 9 / 168 (5.36%) |
| occurrences (all) | 9 | 11 | 12 |
| Pyrexia | | | |
| subjects affected / exposed | 34 / 168 (20.24%) | 44 / 168 (26.19%) | 34 / 168 (20.24%) |
| occurrences (all) | 38 | 51 | 39 |
| Gastrointestinal disorders | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 168 (5.95%) | 22 / 168 (13.10%) | 13 / 168 (7.74%) |
| occurrences (all) | 14 | 29 | 19 |
| Nausea | | | |
| subjects affected / exposed | 22 / 168 (13.10%) | 16 / 168 (9.52%) | 23 / 168 (13.69%) |
| occurrences (all) | 24 | 19 | 31 |
| Vomiting | | | |
| subjects affected / exposed | 20 / 168 (11.90%) | 19 / 168 (11.31%) | 18 / 168 (10.71%) |
| occurrences (all) | 23 | 24 | 20 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 10 / 168 (5.95%) | 6 / 168 (3.57%) | 7 / 168 (4.17%) |
| occurrences (all) | 14 | 8 | 8 |
| Cough | | | |
| subjects affected / exposed | 27 / 168 (16.07%) | 34 / 168 (20.24%) | 35 / 168 (20.83%) |
| occurrences (all) | 37 | 40 | 40 |
| Nasal Congestion | | | |
| subjects affected / exposed | 4 / 168 (2.38%) | 11 / 168 (6.55%) | 6 / 168 (3.57%) |
| occurrences (all) | 4 | 14 | 7 |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 11 / 168 (6.55%) | 12 / 168 (7.14%) | 12 / 168 (7.14%) |
| occurrences (all) | 15 | 14 | 13 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 6 / 168 (3.57%) | 9 / 168 (5.36%) | 9 / 168 (5.36%) |
| occurrences (all) | 7 | 13 | 9 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 9 / 168 (5.36%) | 11 / 168 (6.55%) | 17 / 168 (10.12%) |
| occurrences (all) | 10 | 12 | 23 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 9 / 168 (5.36%) | 6 / 168 (3.57%) | 9 / 168 (5.36%) |
| occurrences (all) | 11 | 6 | 12 |
| Myalgia | | | |
| subjects affected / exposed | 37 / 168 (22.02%) | 13 / 168 (7.74%) | 20 / 168 (11.90%) |
| occurrences (all) | 47 | 14 | 24 |
| Infections and infestations | | | |

| | | | |
|-----------------------------------|-------------------|-------------------|-------------------|
| Bronchitis | | | |
| subjects affected / exposed | 10 / 168 (5.95%) | 7 / 168 (4.17%) | 4 / 168 (2.38%) |
| occurrences (all) | 11 | 7 | 5 |
| Conjunctivitis | | | |
| subjects affected / exposed | 17 / 168 (10.12%) | 8 / 168 (4.76%) | 7 / 168 (4.17%) |
| occurrences (all) | 18 | 8 | 9 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 10 / 168 (5.95%) | 7 / 168 (4.17%) | 10 / 168 (5.95%) |
| occurrences (all) | 11 | 8 | 10 |
| Otitis Media | | | |
| subjects affected / exposed | 18 / 168 (10.71%) | 21 / 168 (12.50%) | 18 / 168 (10.71%) |
| occurrences (all) | 25 | 28 | 23 |
| Otitis Media acute | | | |
| subjects affected / exposed | 4 / 168 (2.38%) | 7 / 168 (4.17%) | 3 / 168 (1.79%) |
| occurrences (all) | 4 | 10 | 3 |
| Pharyngitis | | | |
| subjects affected / exposed | 15 / 168 (8.93%) | 12 / 168 (7.14%) | 10 / 168 (5.95%) |
| occurrences (all) | 18 | 15 | 11 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 20 / 168 (11.90%) | 15 / 168 (8.93%) | 20 / 168 (11.90%) |
| occurrences (all) | 27 | 19 | 22 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 26 / 168 (15.48%) | 25 / 168 (14.88%) | 21 / 168 (12.50%) |
| occurrences (all) | 38 | 29 | 23 |
| Viral Infection | | | |
| subjects affected / exposed | 13 / 168 (7.74%) | 10 / 168 (5.95%) | 17 / 168 (10.12%) |
| occurrences (all) | 13 | 11 | 18 |
| Sinusitis | | | |
| subjects affected / exposed | 11 / 168 (6.55%) | 9 / 168 (5.36%) | 13 / 168 (7.74%) |
| occurrences (all) | 12 | 10 | 14 |

| Non-serious adverse events | Group G | Group H | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 140 / 167 (83.83%) | 138 / 169 (81.66%) | |
| Nervous system disorders | | | |

| | | | |
|---|---------------------------|--------------------------|--|
| Headache subjects affected / exposed occurrences (all) | 38 / 167 (22.75%) 54 | 29 / 169 (17.16%) 41 | |
| General disorders and administration site conditions | | | |
| Chills subjects affected / exposed occurrences (all) | 11 / 167 (6.59%) 13 | 11 / 169 (6.51%) 11 | |
| Fatigue subjects affected / exposed occurrences (all) | 36 / 167 (21.56%) 46 | 20 / 169 (11.83%) 27 | |
| Injection site erythema subjects affected / exposed occurrences (all) | 15 / 167 (8.98%) 19 | 12 / 169 (7.10%) 13 | |
| Injection site induration subjects affected / exposed occurrences (all) | 9 / 167 (5.39%) 11 | 6 / 169 (3.55%) 8 | |
| Injection site Pain subjects affected / exposed occurrences (all) | 103 / 167 (61.68%) 248 | 93 / 169 (55.03%) 220 | |
| Injection site swelling subjects affected / exposed occurrences (all) | 9 / 167 (5.39%) 12 | 8 / 169 (4.73%) 8 | |
| Pyrexia subjects affected / exposed occurrences (all) | 34 / 167 (20.36%) 41 | 26 / 169 (15.38%) 36 | |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 12 / 167 (7.19%) 13 | 16 / 169 (9.47%) 19 | |
| Nausea subjects affected / exposed occurrences (all) | 16 / 167 (9.58%) 18 | 15 / 169 (8.88%) 17 | |
| Vomiting subjects affected / exposed occurrences (all) | 20 / 167 (11.98%) 27 | 21 / 169 (12.43%) 24 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-------------------|-------------------|--|
| Asthma | | | |
| subjects affected / exposed | 11 / 167 (6.59%) | 6 / 169 (3.55%) | |
| occurrences (all) | 18 | 8 | |
| Cough | | | |
| subjects affected / exposed | 40 / 167 (23.95%) | 38 / 169 (22.49%) | |
| occurrences (all) | 47 | 48 | |
| Nasal Congestion | | | |
| subjects affected / exposed | 8 / 167 (4.79%) | 8 / 169 (4.73%) | |
| occurrences (all) | 8 | 9 | |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 14 / 167 (8.38%) | 5 / 169 (2.96%) | |
| occurrences (all) | 14 | 5 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 15 / 167 (8.98%) | 8 / 169 (4.73%) | |
| occurrences (all) | 16 | 9 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 15 / 167 (8.98%) | 11 / 169 (6.51%) | |
| occurrences (all) | 17 | 12 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 8 / 167 (4.79%) | 4 / 169 (2.37%) | |
| occurrences (all) | 8 | 5 | |
| Myalgia | | | |
| subjects affected / exposed | 23 / 167 (13.77%) | 22 / 169 (13.02%) | |
| occurrences (all) | 27 | 30 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | 3 / 169 (1.78%) | |
| occurrences (all) | 7 | 3 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | 6 / 169 (3.55%) | |
| occurrences (all) | 7 | 6 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 167 (5.39%) | 7 / 169 (4.14%) | |
| occurrences (all) | 9 | 7 | |
| Otitis Media | | | |

| | | |
|-----------------------------------|-------------------|-------------------|
| subjects affected / exposed | 23 / 167 (13.77%) | 23 / 169 (13.61%) |
| occurrences (all) | 30 | 35 |
| Otitis Media acute | | |
| subjects affected / exposed | 5 / 167 (2.99%) | 9 / 169 (5.33%) |
| occurrences (all) | 10 | 9 |
| Pharyngitis | | |
| subjects affected / exposed | 6 / 167 (3.59%) | 6 / 169 (3.55%) |
| occurrences (all) | 6 | 6 |
| Pharyngitis streptococcal | | |
| subjects affected / exposed | 13 / 167 (7.78%) | 17 / 169 (10.06%) |
| occurrences (all) | 15 | 19 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 21 / 167 (12.57%) | 22 / 169 (13.02%) |
| occurrences (all) | 29 | 26 |
| Viral Infection | | |
| subjects affected / exposed | 13 / 167 (7.78%) | 12 / 169 (7.10%) |
| occurrences (all) | 16 | 15 |
| Sinusitis | | |
| subjects affected / exposed | 3 / 167 (1.80%) | 9 / 169 (5.33%) |
| occurrences (all) | 3 | 9 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 22 July 2009 | Arthralgia and chills added to systemic reactions. Added explicit statement about parental/guardian completion of diaries. Clarified blinding procedures. Several clarifications added for consistency with other protocols |
| 24 July 2009 | Addition of interim analysis at Day 29. Removed red blood cell count from laboratory assessments and clarified white blood cell count. |
| 10 August 2009 | Local and systemic reactions and applied grading scales adjusted to Center for Biologics Evaluation and Research (CBER) requirements, and language clarified. Safety laboratory assessments list modified to match protocol V112_04 (i.e., analytes to include: hemoglobin, white blood cell count, platelet count, red blood cell count, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), creatinine). Safety laboratory assessments according to standardized toxicity scales, and clarified repeat assessments. Medically attended visits added as a safety endpoint. Definition for new onset of chronic disease added. Clarified populations intended for interim and final immunogenicity analyses. Language clarified to confirm that all concomitant vaccines administered within 21 days of last study vaccination were recorded. Physical assessment procedures at Visit 1 and subsequent visits defined in greater detail. Vital signs and body temperature measurements for each clinic visit added. Several clarifications added. Preferred route of body temperature measurement defined, and conventions for handling measurements obtained via alternate route clarified. Stopping rules added. Minor typographical errors corrected |
| 21 August 2009 | Changed MF59 adjuvant dose-level in the 75%MF59 vaccine groups to 50%. Added lower dose antigen group, and increased sample size by 170 to 1360 (from 1190). Added height and weight assessments. Clarified timing of informed consent. Instructions for handling subjects with fever within 3 days of planned vaccination, or subjects taking analgesics/antipyretics within 24 hours of planned vaccination. Clarified that child birth with healthy outcome is not a SAE. Added medically attended visits to diary cards. Clarified sample handling for serology (immunogenicity). Clarified exclusion criteria #5 and #7. Clarified volume of administration for all vaccine groups. |
| 08 February 2010 | Clarified and outlined the procedures related to antibody persistence. Replaced references to 6 and 12 months with references to Day 202 and Day 387, respectively. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/22418661>