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	• 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			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			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 ≥ 40% and the lower bound of the two-sided 95% CI for the percentages of subjects achieving an HI antibody titer ≥ 1:40 should be ≥ 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 ≥1:40 (Baseline)	11 (6 to 17)	9 (5 to 15)	13 (8 to 19)	11 (6 to 170)
HI titer ≥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 ≥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 ≥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 ≥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 ≥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 ≥1:40 (Baseline)	15 (10 to 22)	9 (5 to 15)	8 (4 to 13)	12 (8 to 19)
HI titer ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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

No statistical analyses for this end point

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-traumtic 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
Pharngitis 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
pharngotonsillitis			

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

subjects affected / exposed	10 / 171 (5.85%)	9 / 168 (5.36%)	7 / 169 (4.14%)
occurrences (all)	15	11	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	38 / 167 (22.75%)	29 / 169 (17.16%)	
occurrences (all)	54	41	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	11 / 167 (6.59%)	11 / 169 (6.51%)	
occurrences (all)	13	11	
Fatigue			
subjects affected / exposed	36 / 167 (21.56%)	20 / 169 (11.83%)	
occurrences (all)	46	27	
Injection site erythema			
subjects affected / exposed	15 / 167 (8.98%)	12 / 169 (7.10%)	
occurrences (all)	19	13	
Injection site induration			
subjects affected / exposed	9 / 167 (5.39%)	6 / 169 (3.55%)	
occurrences (all)	11	8	
Injection site Pain			
subjects affected / exposed	103 / 167 (61.68%)	93 / 169 (55.03%)	
occurrences (all)	248	220	
Injection site swelling			
subjects affected / exposed	9 / 167 (5.39%)	8 / 169 (4.73%)	
occurrences (all)	12	8	
Pyrexia			
subjects affected / exposed	34 / 167 (20.36%)	26 / 169 (15.38%)	
occurrences (all)	41	36	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 167 (7.19%)	16 / 169 (9.47%)	
occurrences (all)	13	19	
Nausea			
subjects affected / exposed	16 / 167 (9.58%)	15 / 169 (8.88%)	
occurrences (all)	18	17	
Vomiting			
subjects affected / exposed	20 / 167 (11.98%)	21 / 169 (12.43%)	
occurrences (all)	27	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, redblood 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