Clinical trial results:
A Phase II, Randomized, Controlled, Open Label, Single-Center Study to Evaluate the Immunogenicity, Safety and Tolerability of Fluad-H5N1 and Seasonal Influenza Vaccine in Adult Subjects.

Summary

EudraCT number	2014-004515-37
Trial protocol	Outside EU/EEA
Global end of trial date	18 December 2008

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	14 January 2015
Version creation reason	• Correction of full data set Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required. Moreover, a change in system user for this study is necessary.

Trial information

Trial identification

Sponsor protocol code	V87P5

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00481065
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics GmbH & Co. KG
Sponsor organisation address	Postfach 1630, Marburg, Germany, 35006
Public contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 December 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the magnitude of antibody responses to two or three doses of Fluad-H5N1 (H5N1 adjuvanted) influenza vaccine and seasonal Agrippal.

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice (GCP), and the applicable regulatory requirement(s) for the country in which the trial was conducted according to International Conference on Harmonization (ICH) guidelines, and applicable Standard Operating Procedures (SOPs).

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	30 April 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 405
Worldwide total number of subjects	405
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)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	405
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 1 site in Columbia.

Pre-assignment

Screening details:

All subjects enrolled were included in the trial. A total of 405 subjects was enrolled and randomized into 8 groups in this study. The participant flow data are from the all randomized set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Concomitant Alone

Arm description:

1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1 then 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Arm type	Experimental
Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two 0.5mL doses

Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

one 0.5mL dose

Arm title	Concomitant+Mixed

Arm description:

1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Arm type	Experimental
Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two 0.5mL doses

one 1mL dose of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

one 0.5mL dose

Arm title	Concomitant+MF59-eH5N1

Arm description:

1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Arm type	Experimental
Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two 0.5mL doses
one 1mL dose of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

one 0.5mL dose

Arm title	Mixed

Arm description:

1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1 and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Arm type	Experimental
Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

two 1mL doses of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

two 1mL doses of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Arm title	Mixed + Mixed

Arm description:

1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, day 22, and day 382

Arm type	Experimental
Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

three 1mL doses of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

three 1mL doses of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Arm title	Mixed+MF59-eH5N1

Arm description:

1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Arm type	Experimental
Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two 1mL doses of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two 1mL doses of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine
One 0.5mL dose of Adjuvanted monovalent H5N1 influenza virus vaccine

Arm title	MF59-eH5N1+eTIV_a

Arm description:

1 dose of MF59-eH5N1 on day 1, 1 dose of eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Arm type	Experimental
Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	Aflunov
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5mL dose of Adjuvanted monovalent H5N1 influenza virus vaccine
One 1mL dose of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza

virus vaccine

Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5mL dose of Trivalent influenza virus vaccine
One 1mL dose of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Arm title	eTIV_a+MF59-eH5N1

Arm description:

1 dose of eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Arm type	Experimental
Investigational medicinal product name	Adjuvanted monovalent H5N1 influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5mL dose of Adjuvanted monovalent H5N1 influenza virus vaccine
One 1mL dose of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Investigational medicinal product name	Trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5mL dose of Trivalent influenza virus vaccine
One 1mL dose of mixed Adjuvanted monovalent H5N1 influenza virus vaccine and Trivalent influenza virus vaccine

Number of subjects in period 1	Concomitant Alone	Concomitant+Mixed	Concomitant+MF59-eH5N1
Started	51	50	51
Completed	29	33	32
Not completed	22	17	19
Consent withdrawn by subject	11	12	7
Adverse Event	1	1	3
Death	-	-	-
Inappropriate enrolment	4	-	2
Lost to follow-up	4	2	4
Unable to Classify	-	1	2
Protocol deviation	2	1	1
Administrative reason	-	-	-

Number of subjects in period 1	Mixed	Mixed + Mixed	Mixed+MF59-eH5N1
Started	52	51	51
Completed	37	28	27
Not completed	15	23	24
Consent withdrawn by subject	11	13	12
Adverse Event	-	1	-
Death	-	1	-
Inappropriate enrolment	-	2	1
Lost to follow-up	3	3	3
Unable to Classify	-	1	-
Protocol deviation	1	2	6
Administrative reason	-	-	2

Number of subjects in period 1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Started	50	49
Completed	34	30
Not completed	16	19
Consent withdrawn by subject	9	10
Adverse Event	1	1
Death	-	-
Inappropriate enrolment	-	1
Lost to follow-up	2	5
Unable to Classify	-	-
Protocol deviation	3	2
Administrative reason	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Concomitant Alone
Reporting group description:	
1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1 then 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Concomitant+Mixed
Reporting group description:	
1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Concomitant+MF59-eH5N1
Reporting group description:	
1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Mixed
Reporting group description:	
1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1 and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Mixed + Mixed
Reporting group description:	
1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, day 22, and day 382	
Reporting group title	Mixed+MF59-eH5N1
Reporting group description:	
1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	MF59-eH5N1+eTIV_a
Reporting group description:	
1 dose of MF59-eH5N1 on day 1, 1 dose of eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	eTIV_a+MF59-eH5N1
Reporting group description:	
1 dose of eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	

Reporting group values	Concomitant Alone	Concomitant+Mixed	Concomitant+MF59-eH5N1
Number of subjects	51	50	51
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	29	29.4	29.5
standard deviation	± 6.2	± 5.8	± 6.5
Gender categorical			
Units: Subjects			
Female	42	31	36
Male	9	19	15

Reporting group values	Mixed	Mixed + Mixed	Mixed+MF59-eH5N1
Number of subjects	52	51	51
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	29.8	29.6	28.8
standard deviation	± 6.8	± 6.1	± 6.2
Gender categorical			
Units: Subjects			
Female	30	36	39
Male	22	15	12

Reporting group values	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1	Total
Number of subjects	50	49	405
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	27.9	30.1	
standard deviation	± 6.2	± 6.2	-

Gender categorical Units: Subjects			
Female	30	32	276
Male	20	17	129

Subject analysis sets

Subject analysis set title	Full Analysis Set – Primary Immunogenicity
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled population who actually received at least one dose of study vaccination, provided at least one evaluable serum sample both before and after baseline, provided immunogenicity and safety results for the primary course of vaccination (up to day 43).

Subject analysis set title	Full Analysis Set – Persistence Immunogenicity
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled population who actually received at least one dose of study vaccination, provided at least one evaluable serum sample both before and after baseline, provided immunogenicity and safety results for the persistence period (day 43 to day 382).

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All enrolled and randomized subjects who actually received a study vaccination and provided post-baseline safety data.

Subject analysis set title	All Enrolled Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects enrolled in this study irrespective of whether they have been randomized or not.

Subject analysis set title	Full Analysis Set – Booster Immunogenicity
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled population who actually received at least one dose of study vaccination, provided at least one evaluable serum sample both before and after baseline, provided immunogenicity and safety results after booster vaccination (day 382 to day 403).

Reporting group values	Full Analysis Set – Primary Immunogenicity	Full Analysis Set – Persistence Immunogenicity	Safety Set
Number of subjects	380	266	401
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			

standard deviation	±	±	±

Gender categorical Units: Subjects			
Female Male			

Reporting group values	All Enrolled Population	Full Analysis Set – Booster Immunogenicity	
Number of subjects	405	265	
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	29.3		
standard deviation	± 6.2	±	
Gender categorical Units: Subjects			
Female	276		
Male	129		

End points

End points reporting groups

Reporting group title	Concomitant Alone
Reporting group description:	
1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1 then 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Concomitant+Mixed
Reporting group description:	
1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Concomitant+MF59-eH5N1
Reporting group description:	
1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Mixed
Reporting group description:	
1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1 and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	Mixed + Mixed
Reporting group description:	
1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, day 22, and day 382	
Reporting group title	Mixed+MF59-eH5N1
Reporting group description:	
1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	MF59-eH5N1+eTIV_a
Reporting group description:	
1 dose of MF59-eH5N1 on day 1, 1 dose of eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Reporting group title	eTIV_a+MF59-eH5N1
Reporting group description:	
1 dose of eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382	
Subject analysis set title	Full Analysis Set – Primary Immunogenicity
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the enrolled population who actually received at least one dose of study vaccination, provided at least one evaluable serum sample both before and after baseline, provided immunogenicity and safety results for the primary course of vaccination (up to day 43).	
Subject analysis set title	Full Analysis Set – Persistence Immunogenicity
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the enrolled population who actually received at least one dose of study vaccination, provided at least one evaluable serum sample both before and after baseline, provided immunogenicity and safety results for the persistence period (day 43 to day 382).	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All enrolled and randomized subjects who actually received a study vaccination and provided post-baseline safety data.	
Subject analysis set title	All Enrolled Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects enrolled in this study irrespective of whether they have been randomized or not.

Subject analysis set title	Full Analysis Set – Booster Immunogenicity
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the enrolled population who actually received at least one dose of study vaccination, provided at least one evaluable serum sample both before and after baseline, provided immunogenicity and safety results after booster vaccination (day 382 to day 403).

Primary: 1. Percentages of Subjects Who Responded to Two or Three Doses of MF59-eH5N1 Influenza Vaccine

End point title	1. Percentages of Subjects Who Responded to Two or Three Doses of MF59-eH5N1 Influenza Vaccine[1]

End point description:

Seroconversion (serocon.) is defined as negative pre-vaccination serum (titer <10 for HI [Haemagglutination Inhibition], area ≤4 mm2 for SRH [Single Radial Haemolysis]) / positive post-vaccination titer (titer ≥ 40 for HI, area ≥ 25 mm2 for SRH).
Significant increase in antibody titer is defined as at least a fourfold increase for HI or at least 50% increase in the SRH area from non-negative pre-vaccination serum (HI ≥ 10, SRH>4mm2).
Seroprotection is defined as a HI titer ≥40 and a SRH area ≥25 mm2.
The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second and third vaccinations (day 43 and day 403)

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: There were no statistical analysis done.

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	47	50
Units: Percentages of Subjects				
number (confidence interval 95%)				
HI seroprot. (day1) N=46,48,47,50,49,48,48,44	0 (0 to 8)	2 (0.053 to 11)	0 (0 to 8)	4 (0 to 14)
HI serocon. (2nd vacc) N=46,48,46,49,48,48,47,43	26 (14 to 41)	69 (54 to 81)	80 (66 to 91)	27 (15 to 41)
HI seroprot. (2nd vacc) N=46,48,46,49,48,48,47,43	26 (14 to 41)	71 (56 to 83)	80 (66 to 91)	29 (17 to 43)
HI serocon. (3rd vacc) N=23,25,28,35,25,20,28,25	74 (52 to 90)	60 (39 to 79)	93 (76 to 99)	54 (37 to 71)
HI seroprot. (3rd vacc) N=24,25,28,35,25,20,28,25	75 (53 to 90)	60 (39 to 79)	93 (76 to 99)	57 (39 to 74)
SRH seroprot. (day 1) N=46,48,47,49,47,47,48,43)	7 (1 to 18)	13 (5 to 25)	2 (0.054 to 11)	8 (2 to 20)
SRH serocon. (2nd vacc) N=46,48,46,49,46,47,47,42	30 (18 to 46)	79 (65 to 90)	93 (82 to 99)	22 (12 to 37)
SRH seroprot. (2nd vacc) N=46,48,46,50,48,48,47,43	37 (23 to 52)	83 (70 to 93)	93 (82 to 99)	28 (16 to 42)
SRH serocon. (3rd vacc) N=25,25,28,35,25,20,28,25	96 (80 to 100)	80 (59 to 93)	96 (82 to 100)	71 (54 to 85)
SRH seroprot. (3rd vacc) N=25,25,28,35,25,20,28,25	100 (86 to 100)	84 (64 to 95)	96 (82 to 100)	77 (60 to 90)
MN ≥40 (day 1) N=46,48,47,50,49,48,48,44)	2 (0.055 to 12)	4 (1 to 14)	2 (0.054 to 11)	4 (0 to 14)
MN ≥40 (2nd vacc) N=46,48,46,50,48,48,47,43	30 (18 to 46)	75 (60 to 86)	96 (85 to 99)	32 (20 to 47)

MN ≥40 (3rd vacc) N=25,25,28,35,25,20,28,25	96 (80 to 100)	96 (80 to 100)	100 (88 to 100)	89 (73 to 97)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	48	48	44
Units: Percentages of Subjects				
number (confidence interval 95%)				
HI seroprot. (day1) N=46,48,47,50,49,48,48,44	2 (0.052 to 11)	0 (0 to 7)	0 (0 to 7)	0 (0 to 8)
HI serocon. (2nd vacc) N=46,48,46,49,48,48,47,43	65 (49 to 78)	71 (56 to 83)	40 (26 to 56)	51 (35 to 67)
HI seroprot. (2nd vacc) N=46,48,46,49,48,48,47,43	67 (58 to 80)	71 (56 to 83)	40 (26 to 56)	51 (35 to 67)
HI serocon. (3rd vacc) N=23,25,28,35,25,20,28,25	64 (43 to 82)	65 (41 to 85)	86 (67 to 96)	64 (43 to 82)
HI seroprot. (3rd vacc) N=24,25,28,35,25,20,28,25	64 (43 to 82)	70 (46 to 88)	86 (37 to 96)	64 (43 to 82)
SRH seroprot. (day 1) N=46,48,47,49,47,47,48,43)	9 (2 to 20)	13 (5 to 26)	8 (2 to 20)	12 (4 to 25)
SRH serocon. (2nd vacc) N=46,48,46,49,46,47,47,42	67 (52 to 80)	81 (67 to 91)	49 (34 to 64)	60 (43 to 74)
SRH seroprot. (2nd vacc) N=46,48,46,50,48,48,47,43	73 (58 to 85)	88 (75 to 95)	55 (40 to 70)	67 (51 to 81)
SRH serocon. (3rd vacc) N=25,25,28,35,25,20,28,25	48 (28 to 69)	60 (36 to 81)	64 (44 to 81)	64 (43 to 82)
SRH seroprot. (3rd vacc) N=25,25,28,35,25,20,28,25	44 (24 to 65)	75 (51 to 91)	82 (63 to 94)	76 (55 to 91)
MN ≥40 (day 1) N=46,48,47,50,49,48,48,44)	2 (0.052 to 11)	2 (0.053 to 11)	2 (0.053 to 11)	2 (0.058 to 12)
MN ≥40 (2nd vacc) N=46,48,46,50,48,48,47,43	75 (60 to 86)	92 (80 to 98)	51 (36 to 66)	47 (31 to 62)
MN ≥40 (3rd vacc) N=25,25,28,35,25,20,28,25	88 (69 to 97)	100 (83 to 100)	93 (76 to 99)	92 (74 to 99)

Statistical analyses

No statistical analyses for this end point

Primary: 2. Geometric Mean Ratio After Two or Three Vaccinations of MF59-eH5N1 Influenza Vaccine

End point title	2. Geometric Mean Ratio After Two or Three Vaccinations of MF59-eH5N1 Influenza Vaccine[2]

End point description:

Geometric mean Ratio (GMR) was calculated for the haemagglutination inhibition (HI), microneutralization (MN) and single-radial haemolysis (SRH) results as well as the associated 95% confidence intervals. GMR was calculated as 21 days after second and third vaccinations over day 1. The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second and third vaccinations (day 43 and day 403)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	46	50
Units: Ratios				
geometric mean (confidence interval 95%)				
HI (2nd vacc) N=46,48,46,49,48,48,47,43	2.11 (1.29 to 3.46)	12 (7.09 to 19)	23 (14 to 37)	2.16 (1.33 to 3.49)
HI (3rd vacc) N=24,25,28,35,25,20,28,25	34 (15 to 76)	17 (7.82 to 37)	93 (44 to 197)	10 (5.36 to 20)
SRH (2nd vacc) N=46,48,46,49,46,47,47,42	1.82 (1.35 to 2.44)	5.32 (3.98 to 7.09)	9.64 (7.17 to 13)	1.58 (1.19 to 2.11)
SRH (3rd vacc) N=25,25,28,35,23,19,28,24	9.92 (6.73 to 15)	6.22 (4.25 to 9.12)	11 (7.47 to 16)	5.13 (3.69 to 7.13)
MN (2nd vacc) N=46,48,46,50,48,48,47,43	2.12 (1.54 to 2.91)	7.64 (5.61 to 10)	13 (9.45 to 18)	2.15 (1.59 to 2.92)
MN (3rd vacc) N=25,25,28,35,25,20,28,25	38 (23 to 64)	39 (23 to 64)	66 (40 to 109)	16 (10 to 25)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	48	47	43
Units: Ratios				
geometric mean (confidence interval 95%)				
HI (2nd vacc) N=46,48,46,49,48,48,47,43	9.52 (5.86 to 15)	14 (8.32 to 22)	2.96 (1.81 to 4.86)	5.34 (3.2 to 8.91)
HI (3rd vacc) N=24,25,28,35,25,20,28,25	9.89 (4.5 to 22)	21 (8.56 to 49)	66 (31 to 139)	12 (5.53 to 26)
SRH (2nd vacc) N=46,48,46,49,46,47,47,42	4.25 (3.16 to 5.71)	6.04 (4.5 to 8.11)	2.9 (2.16 to 3.88)	3.26 (2.39 to 4.44)
SRH (3rd vacc) N=25,25,28,35,23,19,28,24	3.1 (2.07 to 4.65)	6.76 (4.33 to 11)	7.17 (4.95 to 10)	4.55 (3.08 to 6.74)
MN (2nd vacc) N=46,48,46,50,48,48,47,43	6.79 (4.98 to 9.26)	11 (8.04 to 15)	3.86 (2.82 to 5.29)	3.49 (2.52 to 4.84)
MN (3rd vacc) N=25,25,28,35,25,20,28,25	13 (8 to 23)	23 (13 to 41)	58 (36 to 95)	21 (12 to 35)

Statistical analyses

No statistical analyses for this end point

Primary: 3. Percentages of Subjects Who Responded to Two Vaccinations of the Seasonal eTIV_a Influenza Vaccine (Strain H1N1)

End point title	3. Percentages of Subjects Who Responded to Two Vaccinations of the Seasonal eTIV_a Influenza Vaccine (Strain

	H1N1)[3]

End point description:

Seroconversion: negative pre-vaccination serum (HI titer <10, SRH area ≤ 4 mm2)/positive post-vaccination titer (HI titer ≥10) or at least 50% increase in the SRH area.
Seroprotection is defined as a HI titer ≥40 and a SRH area ≥25 mm2.
The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second vaccination (day 43)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	47	50
Units: Percentages of Subjects				
number (confidence interval 95%)				
HI seroprot. (day1)	28 (16 to 43)	38 (24 to 53)	34 (21 to 49)	46 (32 to 61)
HI seroconv. (day43) N=46,48,46,50,48,48,47,43	72 (57 to 84)	73 (58 to 85)	78 (64 to 89)	58 (43 to 72)
HI seroprot. (day43) N=46,48,46,50,48,48,47,43	80 (66 to 91)	94 (83 to 99)	93 (82 to 99)	78 (64 to 88)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	48	48	44
Units: Percentages of Subjects				
number (confidence interval 95%)				
HI seroprot. (day1)	31 (18 to 45)	40 (26 to 55)	50 (35 to 65)	45 (30 to 61)
HI seroconv. (day43) N=46,48,46,50,48,48,47,43	77 (63 to 88)	77 (63 to 88)	62 (46 to 75)	72 (56 to 85)
HI seroprot. (day43) N=46,48,46,50,48,48,47,43	92 (80 to 98)	85 (72 to 94)	91 (80 to 98)	93 (81 to 99)

Statistical analyses

No statistical analyses for this end point

Primary: 4. Percentages of Subjects Who Responded to Two or Three Vaccinations of seasonal eTIV_a Influenza Vaccine (Strain H3N2)

End point title	4. Percentages of Subjects Who Responded to Two or Three Vaccinations of seasonal eTIV_a Influenza Vaccine (Strain H3N2)[4]

End point description:

Seroconversion: negative pre-vaccination serum (HI titer <10, SRH area ≤4 mm2)/positive post-vaccination titer (HI titer ≥10) or at least 50% increase in the SRH area.
Seroprotection is defined as a HI titer ≥40 and a SRH area ≥25 mm2.

The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second and third vaccinations (day 43 and day 403)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	47	50
Units: Percentages of Subjects				
number (confidence interval 95%)				
HI seroprot. (day1)	43 (29 to 59)	46 (31 to 61)	30 (17 to 45)	46 (32 to 61)
HI seroconv. (2nd vacc) N=46,48,46,49,48,48,47,43	50 (35 to 65)	75 (60 to 86)	76 (61 to 87)	70 (55 to 82)
HI seroprot. (2nd vacc) N=46,48,46,50,48,48,47,43	85 (71 to 94)	96 (86 to 99)	96 (85 to 99)	98 (89 to 100)
HI seroconv. (3rd vacc) N=25,25,28,35,25,20,28,25	76 (55 to 91)	80 (59 to 93)	93 (76 to 99)	86 (70 to 95)
HI seroprot. (3rd vacc) N=25,25,28,35,25,20,28,25	100 (86 to 100)	100 (86 to 100)	100 (88 to 100)	100 (90 to 100)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	48	48	44
Units: Percentages of Subjects				
number (confidence interval 95%)				
HI seroprot. (day1)	53 (38 to 67)	46 (31 to 61)	25 (14 to 40)	50 (35 to 65)
HI seroconv. (2nd vacc) N=46,48,46,49,48,48,47,43	83 (70 to 93)	83 (70 to 93)	74 (60 to 86)	67 (51 to 81)
HI seroprot. (2nd vacc) N=46,48,46,50,48,48,47,43	100 (93 to 100)	100 (93 to 100)	100 (92 to 100)	93 (81 to 99)
HI seroconv. (3rd vacc) N=25,25,28,35,25,20,28,25	72 (51 to 88)	85 (62 to 97)	89 (72 to 98)	84 (64 to 95)
HI seroprot. (3rd vacc) N=25,25,28,35,25,20,28,25	100 (86 to 100)	100 (83 to 100)	100 (88 to 100)	100 (86 to 100)

Statistical analyses

No statistical analyses for this end point

Primary: 5. Percentages of Subjects Who Responded to Two or Three Vaccinations of seasonal eTIV_a Influenza Vaccine (Strain B)

End point title	5. Percentages of Subjects Who Responded to Two or Three Vaccinations of seasonal eTIV_a Influenza Vaccine (Strain B)[5]

End point description:

Seroconversion: negative pre-vaccination serum (HI titer <10, SRH area ≤4 mm2)/positive post-

vaccination titer (HI titer ≥10) or at least 50% increase in the SRH area.
Seroprotection is defined as a HI titer ≥40 and a SRH area ≥25 mm2.
The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second and third vaccinations (day 43 and day 403)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	47	50
Units: Percentages of subjects				
number (confidence interval 95%)				
HI seroprot. (day1)	11 (4 to 24)	8 (2 to 20)	13 (5 to 26)	20 (10 to 34)
HI seroconv. (2nd vacc) N=46,48,46,50,48,48,47,43	80 (66 to 91)	79 (65 to 90)	78 (64 to 89)	82 (69 to 91)
HI seroprot. (2nd vacc) N=46,48,46,50,48,48,47,43	87 (74 to 95)	90 (77 to 97)	91 (79 to 98)	92 (81 to 98)
HI seroconv. (3rd vacc) N=25,25,28,35,25,20,28,25	76 (55 to 91)	68 (46 to 85)	68 (48 to 84)	77 (60 to 90)
HI seroprot. (3rd vacc) N=25,25,28,35,25,20,28,25	88 (69 to 97)	84 (64 to 95)	79 (59 to 92)	89 (73 to 97)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	48	48	44
Units: Percentages of subjects				
number (confidence interval 95%)				
HI seroprot. (day1)	4 (0 to 14)	19 (9 to 33)	25 (14 to 40)	11 (4 to 24)
HI seroconv. (2nd vacc) N=46,48,46,50,48,48,47,43	85 (72 to 94)	73 (58 to 85)	77 (62 to 88)	65 (49 to 79)
HI seroprot. (2nd vacc) N=46,48,46,50,48,48,47,43	92 (80 to 98)	94 (83 to 99)	94 (82 to 99)	74 (59 to 86)
HI seroconv. (3rd vacc) N=25,25,28,35,25,20,28,25	60 (39 to 79)	65 (41 to 85)	39 (22 to 59)	60 (39 to 79)
HI seroprot. (3rd vacc) N=25,25,28,35,25,20,28,25	72 (51 to 88)	90 (68 to 99)	61 (41 to 78)	80 (59 to 93)

Statistical analyses

No statistical analyses for this end point

Primary: 6. Geometric Mean Ratio After Two Doses of the Seasonal eTIV_a Influenza Vaccine (Strain H1N1)

End point title	6. Geometric Mean Ratio After Two Doses of the Seasonal eTIV_a Influenza Vaccine (Strain H1N1)[6]

End point description:

For each vaccine group, the least squares GMRs were calculated for the haemagglutination inhibition (HI) results as well as the associated 95% confidence intervals. GMR was calculated over day 1.
The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second vaccination (day 43)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	46	50
Units: Ratios				
geometric mean (confidence interval 95%)				
GMR (Strain H1N1, Day 43/Day1)	15 (9.54 to 23)	13 (8.43 to 20)	14 (8.82 to 21)	6.77 (4.46 to 10)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	48	47	43
Units: Ratios				
geometric mean (confidence interval 95%)				
GMR (Strain H1N1, Day 43/Day1)	12 (7.81 to 18)	10 (6.69 to 16)	6.23 (4.03 to 9.61)	11 (6.76 to 17)

Statistical analyses

No statistical analyses for this end point

Primary: 7. Geometric Mean Ratio After Two or Three Doses of the Seasonal eTIV_a Influenza Vaccine (Strain H3N2)

End point title	7. Geometric Mean Ratio After Two or Three Doses of the Seasonal eTIV_a Influenza Vaccine (Strain H3N2)[7]

End point description:

For each vaccine group, the least squares GMRs were calculated for the haemagglutination inhibition (HI) results as well as the associated 95% confidence intervals. GMR was calculated over day 1.
The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second and third vaccinations (day 43 and day 403)

Notes:

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

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	47	50
Units: Ratios				
geometric mean (confidence interval 95%)				
HI GMR (2nd vacc) N=46,48,46,50,48,48,47,43	6.01 (4.01 to 9.01)	9.72 (6.54 to 14)	9.34 (6.22 to 14)	11 (7.54 to 16)
HI GMR (3rd vacc) N=25,25,28,35,25,20,28,25	17 (9.56 to 29)	10 (6.04 to 18)	17 (9.86 to 28)	18 (11 to 29)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	48	48	44
Units: Ratios				
geometric mean (confidence interval 95%)				
HI GMR (2nd vacc) N=46,48,46,50,48,48,47,43	11 (7.26 to 16)	10 (6.92 to 15)	11 (7.25 to 16)	7.54 (4.96 to 11)
HI GMR (3rd vacc) N=25,25,28,35,25,20,28,25	8.92 (5.12 to 16)	11 (5.8 to 20)	17 (10 to 29)	13 (7.64 to 23)

Statistical analyses

No statistical analyses for this end point

Primary: 8. Geometric Mean Ratio After Two or Three Doses of the Seasonal eTIV_a Influenza Vaccine (Strain B)

End point title	8. Geometric Mean Ratio After Two or Three Doses of the Seasonal eTIV_a Influenza Vaccine (Strain B)[8]

End point description:

For each vaccine group, the least squares GMRs were calculated for the haemagglutination inhibition (HI) results as well as the associated 95% confidence intervals. GMR was calculated over day 1.
The analysis was done on the full analysis set (FAS).

End point type	Primary

End point timeframe:

21 days after second and third vaccinations (day 43 and day 403)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	48	47	50
Units: Ratios				
geometric mean (confidence interval 95%)				

HI GMR (2nd vacc) N=46,48,46,50,48,48,47,43	11 (7.85 to 17)	13 (9.01 to 19)	10 (6.94 to 15)	10 (7.22 to 15)
HI GMR (3rd vacc) N=25,25,28,35,25,20,28,25	8.85 (5.86 to 13)	5.47 (3.64 to 8.22)	7.95 (5.37 to 12)	7.17 (5.05 to 10)

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	48	48	44
Units: Ratios				
geometric mean (confidence interval 95%)				
HI GMR (2nd vacc) N=46,48,46,50,48,48,47,43	17 (12 to 25)	8.77 (6.07 to 13)	10 (6.97 to 15)	8 (5.44 to 12)
HI GMR (3rd vacc) N=25,25,28,35,25,20,28,25	5.29 (3.51 to 8)	5.1 (3.22 to 8.06)	4.17 (2.82 to 6.18)	4.26 (2.84 to 6.4)

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of Subjects Reporting Local and Systemic Reactions by Vaccination

End point title	9. Number of Subjects Reporting Local and Systemic Reactions by Vaccination

End point description:

To evaluate the safety of the administration of two or three vaccinations of MF59-eH5N1(H5N1 adjuvanted) influenza vaccine, either given sequentially, concomitantly or mixed extemporaneously with seasonal eTIV_a influenza vaccine.
The analysis was done on the safety set.

End point type	Secondary

End point timeframe:

for 21 days after 2nd and 3rd vaccinations (from day 22 to day43 and from day 382 to day 403)

End point values	Concomitant Alone	Concomitant+ Mixed	Concomitant+ MF59-eH5N1	Mixed
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	51
Units: Subjects				
Erythema (N=0,48,47,0,48,47,47,43) 2nd vacc	0	8	8	0
Induration(N=0,48,47,0,48,47,47,43) 2nd vacc	0	2	3	0
Swelling(N=0,47,47,0,48,47,47,43) 2nd vacc	0	2	5	0
Ecchymosis(N=0,48,47,0,48,47,47,43) 2nd vacc	0	0	0	0
Pain(N=0,48,47,0,48,47,47,43) 2nd vacc	0	21	16	0

Erythema(N=31,33,36,39,31,29,34,31) 3rd vacc	8	4	9	9
Induration(N=31,33,36,39,31,28,34,31) 3rd vacc	6	6	14	9
Swelling(N=31,33,36,39,31,29,34,31) 3rd vacc	5	3	9	2
Ecchymosis(N=31,33,36,39,31,29,34,31) 3rd vacc	2	1	1	1
Pain(N=31,33,36,39,31,29,34,31) 3rd vacc	20	16	21	23
Chills(N=0,48,47,0,48,45,47,42) 2nd vacc	0	0	1	0
Chills(31,33,36,39,31,29,34,32) 3rd vacc	3	0	6	3
Malaise(N=0,48,47,0,48,45,47,42) 2nd vacc	0	2	4	0
Malaise(N=31,33,36,39,31,29,34,32) 3rd vacc	6	5	9	10
Myalgia(N=0,48,47,0,48,45,47,42) 2nd vacc	0	8	7	0
Myalgia(N=30,33,36,39,31,29,34,32) 3rd vacc	12	11	17	13
Arthralgia(N=0,48,47,0,48,45,47,42) 2nd vacc	0	0	3	0
Arthralgia(N=31,33,36,39,31,29,34,32) 3rd vacc	2	3	5	4
Headache(N=0,48,47,0,48,45,47,42) 2nd vacc	0	2	5	0
Headache (N=31,32,36,39,31,29,34,32) 3rd vacc	8	7	11	7
Sweating(N=0,48,47,0,48,45,47,42) 2nd vacc	0	0	1	0
Sweating(N=31,33,36,39,31,29,34,32) 3rd vacc	2	0	2	2
Fatigue(N=0,48,47,0,48,45,47,42) 2nd vacc	0	1	0	0
Fatigue(N=31,33,36,39,31,29,34,32) 3rd vacc	2	1	3	1
Nausea(N=0,48,47,0,48,45,47,42) 2nd vacc	0	0	1	0
Nausea(N=31,33,36,39,31,29,34,32) 3rd vacc	1	1	3	2
Fever ≥38C(N=0,47,47,0,48,45,46,42) 2nd vacc	0	0	0	0
Fever ≥38C (N=31,33,36,39,31,29,34,32) 3rd vacc	2	0	0	0

End point values	Mixed + Mixed	Mixed+MF59-eH5N1	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	50	49	49
Units: Subjects				
Erythema (N=0,48,47,0,48,47,47,43) 2nd vacc	8	8	7	5
Induration(N=0,48,47,0,48,47,47,43) 2nd vacc	3	2	1	3
Swelling(N=0,47,47,0,48,47,47,43) 2nd vacc	4	1	1	1

Ecchymosis(N=0,48,47,0,48,47,47,43) 2nd vacc	1	1	1	0
Pain(N=0,48,47,0,48,47,47,43) 2nd vacc	20	18	12	16
Erythema(N=31,33,36,39,31,29,34,31) 3rd vacc	12	7	6	11
Induration(N=31,33,36,39,31,28,34,31) 3rd vacc	9	9	7	8
Swelling(N=31,33,36,39,31,29,34,31) 3rd vacc	7	8	6	5
Ecchymosis(N=31,33,36,39,31,29,34,31) 3rd vacc	1	1	2	3
Pain(N=31,33,36,39,31,29,34,31) 3rd vacc	20	17	17	15
Chills(N=0,48,47,0,48,45,47,42) 2nd vacc	2	4	2	2
Chills(31,33,36,39,31,29,34,32) 3rd vacc	4	0	3	0
Malaise(N=0,48,47,0,48,45,47,42) 2nd vacc	7	6	2	6
Malaise(N=31,33,36,39,31,29,34,32) 3rd vacc	8	7	9	7
Myalgia(N=0,48,47,0,48,45,47,42) 2nd vacc	9	6	3	5
Myalgia(N=30,33,36,39,31,29,34,32) 3rd vacc	12	10	8	13
Arthralgia(N=0,48,47,0,48,45,47,42) 2nd vacc	1	4	2	2
Arthralgia(N=31,33,36,39,31,29,34,32) 3rd vacc	4	3	4	4
Headache(N=0,48,47,0,48,45,47,42) 2nd vacc	6	5	3	4
Headache (N=31,32,36,39,31,29,34,32) 3rd vacc	10	8	5	7
Sweating(N=0,48,47,0,48,45,47,42) 2nd vacc	0	2	1	1
Sweating(N=31,33,36,39,31,29,34,32) 3rd vacc	0	1	0	3
Fatigue(N=0,48,47,0,48,45,47,42) 2nd vacc	1	1	2	2
Fatigue(N=31,33,36,39,31,29,34,32) 3rd vacc	2	2	1	1
Nausea(N=0,48,47,0,48,45,47,42) 2nd vacc	1	1	2	2
Nausea(N=31,33,36,39,31,29,34,32) 3rd vacc	3	0	2	2
Fever ≥38C(N=0,47,47,0,48,45,46,42) 2nd vacc	1	3	0	2
Fever ≥38C (N=31,33,36,39,31,29,34,32) 3rd vacc	0	1	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Percentages of Subjects With Immunogenicity Results After the Booster Vaccination Against the MF59-eH5N1 (H5N1 Adjuvanted) Influenza Vaccine Mixed Extemporaneously With the Seasonal eTIV_a Influenza Vaccine

End point title	10. Percentages of Subjects With Immunogenicity Results After the Booster Vaccination Against the MF59-eH5N1 (H5N1 Adjuvanted) Influenza Vaccine Mixed Extemporaneously With the Seasonal eTIV_a Influenza Vaccine[9]

End point description:

Booster was given on day 382; seroconversion: negative pre-vaccination serum (HI titer <10, SRH area ≤ 4 mm2)/positive post- vaccination titer (HI titer ≥10) or at least 50% increase in SRH area; seroprotection is defined as a HI titer ≥40 and a SRH area ≥25 mm2.
The number of subjects achieving seroconversion or significant increase and seroprotection were taken on day 403 and ratios calculated as Day403/day382 at day 382.
The analysis was done on the full analysis set (FAS).

End point type	Secondary

End point timeframe:

21 days after booster vaccination (day 403)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There were no statistical analysis done.

End point values	Mixed	Mixed + Mixed		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	31		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Seroprotection (HI) - MF59-eH5N1 (N=35,25)	74 (57 to 88)	64 (43 to 82)		
Seroconversion (HI) - MF59-eH5N1 (N=35,25)	71 (54 to 85)	60 (39 to 79)		
Seroprotection (SRH) - MF59-eH5N1 (N=35,25)	57 (39 to 74)	28 (12 to 49)		
Seroconversion (SRH) - MF59-eH5N1 (N=35,25)	60 (42 to 76)	40 (21 to 61)		
Seroprotection (HI) - eTIV_a (H1N1) N=35,25	94 (81 to 99)	96 (80 to 100)		
Seroconversion (HI) - eTIV_a (H1N1) N=35,25	49 (31 to 66)	40 (21 to 61)		
Seroprotection (HI) - eTIV_a (H3N2) N=35,25	100 (90 to 100)	100 (86 to 100)		
Seroconversion (HI) - eTIV_a (H3N2) N=35,25	34 (19 to 52)	20 (7 to 41)		
Seroprotection (HI) - eTIV_a (B) N=35,25	89 (73 to 97)	72 (51 to 88)		
Seroconversion (HI) - eTIV_a (B) N=35,25	17 (7 to 34)	16 (5 to 36)		

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Geometric Mean Ratios After the Booster Vaccination Against the MF59-eH5N1 (H5N1 Adjuvanted) Influenza Vaccine Mixed Extemporaneously With the Seasonal eTIV_a Influenza Vaccine

End point title	11. Geometric Mean Ratios After the Booster Vaccination Against the MF59-eH5N1 (H5N1 Adjuvanted) Influenza Vaccine Mixed Extemporaneously With the Seasonal eTIV_a Influenza Vaccine[10]

End point description:

For each vaccine group, the least squares GMRs were calculated for the HI and SRH results for each time point of the study, as well as the associated 95% confidence intervals. GMR was calculated over day 382 for all time points for the booster dose.
The analysis was done on the full analysis set (FAS).

End point type	Secondary

End point timeframe:

21 days after booster vaccination (day 403)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There were no statistical analysis done.

End point values	Mixed	Mixed + Mixed		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	31		
Units: Ratios				
geometric mean (confidence interval 95%)				
HI (MF59-eH5N1) N=35,25	13 (6.99 to 25)	7.14 (3.4 to 15)		
SRH (MF59-eH5N1) N=35,25	4.88 (3.59 to 6.63)	2.77 (1.93 to 3.98)		
HI (eTIV_a, H1N1) N=35,25	4.85 (3.05 to 7.73)	2.61 (1.51 to 4.51)		
HI (eTIV_a, H3N2) N=35,25	2.62 (1.83 to 3.76)	2.21 (1.44 to 3.39)		
HI (eTIV_a l, B) N=35,25	1.96 (1.55 to 2.48)	1.94 (1.47 to 2.55)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events and serious adverse events were collected for 20 months (the duration of the study).

Adverse event reporting additional description:

The number of subjects included here are from the safety population and not the enrolled population as disclosed in the Demography and Study Termination sections.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	Concomitant Alone

Reporting group description:

1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1 then 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Reporting group title	Concomitant+Mixed

Reporting group description:

1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Reporting group title	Concomitant+MF59-eH5N1

Reporting group description:

1 dose of MF59-eH5N1 into one arm and 1 dose of eTIV_a into the other arm on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Reporting group title	Mixed

Reporting group description:

1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1 and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Reporting group title	Mixed + Mixed

Reporting group description:

1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, day 22, and day 382

Reporting group title	Mixed+MF59-eH5N1

Reporting group description:

1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Reporting group title	MF59-eH5N1+eTIV_a

Reporting group description:

1 dose of MF59-eH5N1 on day 1, 1 dose of eTIV_a on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Reporting group title	eTIV_a+MF59-eH5N1

Reporting group description:

1 dose of eTIV_a on day 1, 1 dose of MF59-eH5N1 on day 22, and 1 dose of MF59-eH5N1 mixed extemporaneously with eTIV_a on day 382

Serious adverse events	Concomitant Alone	Concomitant+Mixed	Concomitant+MF59-eH5N1
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 50 (8.00%)	1 / 50 (2.00%)	2 / 51 (3.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Aspiration Bronchial			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 51 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell small lymphocytic lymphoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ependymoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 51 (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
Injury			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 51 (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
Joint dislocation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 51 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 51 (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
Abortion spontaneous incomplete			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 51 (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
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 51 (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			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 51 (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
Gastrointestinal infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 51 (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
Periorbital cellulitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 51 (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
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 51 (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

Serious adverse events	Mixed	Mixed + Mixed	Mixed+MF59-eH5N1
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 51 (5.88%)	3 / 51 (5.88%)	0 / 50 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from	0	0	0

adverse events			
Investigations			
Aspiration Bronchial			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 50 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell small lymphocytic lymphoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 50 (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
Ependymoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 50 (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
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 50 (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
Injury			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 50 (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
Joint dislocation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 50 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 50 (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
Abortion spontaneous incomplete			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 50 (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			
Vaginal haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 50 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 50 (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
Gastrointestinal infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 50 (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
Periorbital cellulitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 50 (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 / 51 (1.96%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Aspiration Bronchial			

subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell small lymphocytic lymphoma			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ependymoma			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous incomplete			

subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (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			
Vaginal haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (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			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (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 / 49 (0.00%)	0 / 49 (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	Concomitant Alone	Concomitant+Mixed	Concomitant+MF59-eH5N1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 50 (76.00%)	43 / 50 (86.00%)	41 / 51 (80.39%)
Nervous system disorders			
Headache			

subjects affected / exposed	18 / 50 (36.00%)	17 / 50 (34.00%)	22 / 51 (43.14%)
occurrences (all)	27	31	35
Migraine			
subjects affected / exposed	3 / 50 (6.00%)	1 / 50 (2.00%)	0 / 51 (0.00%)
occurrences (all)	3	1	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	5 / 50 (10.00%)	5 / 50 (10.00%)	10 / 51 (19.61%)
occurrences (all)	7	6	10
Fatigue			
subjects affected / exposed	3 / 50 (6.00%)	4 / 50 (8.00%)	5 / 51 (9.80%)
occurrences (all)	4	5	6
Injection site erythema			
subjects affected / exposed	12 / 50 (24.00%)	17 / 50 (34.00%)	17 / 51 (33.33%)
occurrences (all)	16	24	24
Injection Site Haemorrhage			
subjects affected / exposed	3 / 50 (6.00%)	5 / 50 (10.00%)	2 / 51 (3.92%)
occurrences (all)	3	6	2
Injection Site Induration			
subjects affected / exposed	11 / 50 (22.00%)	15 / 50 (30.00%)	21 / 51 (41.18%)
occurrences (all)	13	24	36
Injection site pain			
subjects affected / exposed	29 / 50 (58.00%)	34 / 50 (68.00%)	33 / 51 (64.71%)
occurrences (all)	47	80	75
Injection site swelling			
subjects affected / exposed	8 / 50 (16.00%)	9 / 50 (18.00%)	15 / 51 (29.41%)
occurrences (all)	9	14	26
Malaise			
subjects affected / exposed	15 / 50 (30.00%)	18 / 50 (36.00%)	22 / 51 (43.14%)
occurrences (all)	25	23	27
Pyrexia			
subjects affected / exposed	5 / 50 (10.00%)	1 / 50 (2.00%)	2 / 51 (3.92%)
occurrences (all)	6	1	2
Gastrointestinal disorders			

Gastritis			
subjects affected / exposed	1 / 50 (2.00%)	3 / 50 (6.00%)	0 / 51 (0.00%)
occurrences (all)	1	4	0
Nausea			
subjects affected / exposed	4 / 50 (8.00%)	5 / 50 (10.00%)	6 / 51 (11.76%)
occurrences (all)	4	5	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	3 / 50 (6.00%)	2 / 50 (4.00%)	8 / 51 (15.69%)
occurrences (all)	4	2	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 50 (6.00%)	4 / 50 (8.00%)	11 / 51 (21.57%)
occurrences (all)	3	4	13
Myalgia			
subjects affected / exposed	16 / 50 (32.00%)	24 / 50 (48.00%)	25 / 51 (49.02%)
occurrences (all)	22	38	36
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 50 (6.00%)	1 / 50 (2.00%)	0 / 51 (0.00%)
occurrences (all)	3	1	0
Sinusitis			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	0 / 51 (0.00%)
occurrences (all)	1	1	0
Tonsillitis			
subjects affected / exposed	2 / 50 (4.00%)	2 / 50 (4.00%)	0 / 51 (0.00%)
occurrences (all)	2	2	0

Non-serious adverse events	Mixed	Mixed + Mixed	Mixed+MF59-eH5N1
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	39 / 51 (76.47%)	42 / 51 (82.35%)	43 / 50 (86.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 51 (27.45%)	25 / 51 (49.02%)	19 / 50 (38.00%)
occurrences (all)	17	41	31
Migraine			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	8 / 51 (15.69%)	8 / 51 (15.69%)	8 / 50 (16.00%)
occurrences (all)	9	11	9
Fatigue			
subjects affected / exposed	3 / 51 (5.88%)	5 / 51 (9.80%)	4 / 50 (8.00%)
occurrences (all)	3	6	4
Injection site erythema			
subjects affected / exposed	16 / 51 (31.37%)	21 / 51 (41.18%)	16 / 50 (32.00%)
occurrences (all)	18	29	19
Injection Site Haemorrhage			
subjects affected / exposed	5 / 51 (9.80%)	5 / 51 (9.80%)	3 / 50 (6.00%)
occurrences (all)	5	6	3
Injection Site Induration			
subjects affected / exposed	16 / 51 (31.37%)	15 / 51 (29.41%)	15 / 50 (30.00%)
occurrences (all)	18	18	16
Injection site pain			
subjects affected / exposed	32 / 51 (62.75%)	34 / 51 (66.67%)	32 / 50 (64.00%)
occurrences (all)	48	68	54
Injection site swelling			
subjects affected / exposed	10 / 51 (19.61%)	10 / 51 (19.61%)	10 / 50 (20.00%)
occurrences (all)	10	15	13
Malaise			
subjects affected / exposed	19 / 51 (37.25%)	21 / 51 (41.18%)	21 / 50 (42.00%)
occurrences (all)	24	34	35
Pyrexia			

subjects affected / exposed	4 / 51 (7.84%)	4 / 51 (7.84%)	8 / 50 (16.00%)
occurrences (all)	4	4	11
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	2 / 51 (3.92%)	2 / 51 (3.92%)	1 / 50 (2.00%)
occurrences (all)	2	2	1
Nausea			
subjects affected / exposed	2 / 51 (3.92%)	6 / 51 (11.76%)	4 / 50 (8.00%)
occurrences (all)	2	9	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 51 (3.92%)	2 / 51 (3.92%)	4 / 50 (8.00%)
occurrences (all)	2	2	4
Oropharyngeal pain			
subjects affected / exposed	3 / 51 (5.88%)	2 / 51 (3.92%)	1 / 50 (2.00%)
occurrences (all)	3	2	1
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	4 / 51 (7.84%)	3 / 51 (5.88%)	4 / 50 (8.00%)
occurrences (all)	4	5	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 51 (11.76%)	8 / 51 (15.69%)	9 / 50 (18.00%)
occurrences (all)	7	11	10
Myalgia			
subjects affected / exposed	23 / 51 (45.10%)	24 / 51 (47.06%)	17 / 50 (34.00%)
occurrences (all)	35	41	30
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	1 / 50 (2.00%)
occurrences (all)	1	1	1
Sinusitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			

subjects affected / exposed	0 / 51 (0.00%)	2 / 51 (3.92%)	3 / 50 (6.00%)
occurrences (all)	0	2	3

Non-serious adverse events	MF59-eH5N1+eTIV_a	eTIV_a+MF59-eH5N1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 49 (75.51%)	38 / 49 (77.55%)	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 49 (26.53%)	15 / 49 (30.61%)	
occurrences (all)	20	19	
Migraine			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	5 / 49 (10.20%)	3 / 49 (6.12%)	
occurrences (all)	10	3	
Fatigue			
subjects affected / exposed	4 / 49 (8.16%)	4 / 49 (8.16%)	
occurrences (all)	9	5	
Injection site erythema			
subjects affected / exposed	16 / 49 (32.65%)	21 / 49 (42.86%)	
occurrences (all)	20	23	
Injection Site Haemorrhage			
subjects affected / exposed	3 / 49 (6.12%)	3 / 49 (6.12%)	
occurrences (all)	4	3	
Injection Site Induration			
subjects affected / exposed	10 / 49 (20.41%)	15 / 49 (30.61%)	
occurrences (all)	15	19	
Injection site pain			
subjects affected / exposed	33 / 49 (67.35%)	29 / 49 (59.18%)	
occurrences (all)	53	38	
Injection site swelling			
subjects affected / exposed	9 / 49 (18.37%)	11 / 49 (22.45%)	
occurrences (all)	12	12	
Malaise			

subjects affected / exposed	17 / 49 (34.69%)	14 / 49 (28.57%)	
occurrences (all)	27	21	
Pyrexia			
subjects affected / exposed	2 / 49 (4.08%)	7 / 49 (14.29%)	
occurrences (all)	2	7	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	4 / 49 (8.16%)	1 / 49 (2.04%)	
occurrences (all)	6	1	
Nausea			
subjects affected / exposed	4 / 49 (8.16%)	7 / 49 (14.29%)	
occurrences (all)	9	8	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 49 (2.04%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	2 / 49 (4.08%)	4 / 49 (8.16%)	
occurrences (all)	4	7	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 49 (14.29%)	6 / 49 (12.24%)	
occurrences (all)	13	6	
Myalgia			
subjects affected / exposed	18 / 49 (36.73%)	17 / 49 (34.69%)	
occurrences (all)	30	21	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 49 (2.04%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Sinusitis			

subjects affected / exposed	0 / 49 (0.00%)	3 / 49 (6.12%)	
occurrences (all)	0	3	
Tonsillitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 49 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 January 2008	Change of study design: to do the booster also with a tetravalent vaccine (MF59-EH5N1 mixed extemporaneously with Agrippal® 2007/2008).

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/23536690

http://www.ncbi.nlm.nih.gov/pubmed/21606530