



Clinical trial results:

A Phase III, open-label, non-randomised, multi-centre, single dose study to assess the immunogenicity and safety of GSK Biologicals' Quadrivalent Split Virion Influenza Vaccine (GSK2321138A) Influsplit Tetra (Fluarix Tetra) (2013/2014 season) injected intramuscularly in adults (18 to 60 years) and in the elderly (over 60 years)

Summary

EudraCT number	2013-001094-25
Trial protocol	DE
Global end of trial date	05 August 2013

Results information

Result version number	v2
This version publication date	28 May 2016
First version publication date	25 April 2015
Version creation reason	• Correction of full data set Data (typos) were corrected in the GMT tables (Secondary endpoints).

Trial information

Trial identification

Sponsor protocol code	200188
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01878812
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.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	13 August 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 August 2013
Global end of trial reached?	Yes
Global end of trial date	05 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the humoral response [(anti- Haemagglutinin (HA) antibodies tested by Haemagglutination Inhibition (HI)] against each vaccine strain in adults 18-60 years and >60 years of age, 21 days after vaccination with Fluarix/Influsplit Tetra 2013/2014.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Only eligible subjects that had no contraindications to any components of the vaccines were vaccinated. Subjects were followed-up for xx days after each/last vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 July 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 117
Worldwide total number of subjects	117
EEA total number of subjects	117

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)	60
From 65 to 84 years	57

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Fluarix/Influsplit Tetra® Adult Group

Arm description:

Subjects 18-60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Fluarix/Influsplit Tetra® (2013-2014 season)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the deltoid region of non-dominant arm

Arm title	Fluarix/Influsplit Tetra® Elderly Group
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Arm description:

Subjects >60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Fluarix/Influsplit Tetra® (2013-2014 season)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the deltoid region of non-dominant arm

Number of subjects in period 1	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group
Started	60	57
Completed	60	57

Baseline characteristics

Reporting groups

Reporting group title	Fluarix/Influsplit Tetra® Adult Group
Reporting group description: Subjects 18-60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.	
Reporting group title	Fluarix/Influsplit Tetra® Elderly Group
Reporting group description: Subjects >60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.	

Reporting group values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group	Total
Number of subjects	60	57	117
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	38.7	70.6	
standard deviation	± 12.24	± 6.81	-
Gender categorical Units: Subjects			
Female	32	31	63
Male	28	26	54

End points

End points reporting groups

Reporting group title	Fluarix/Influsplit Tetra® Adult Group
Reporting group description:	
Subjects 18-60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.	
Reporting group title	Fluarix/Influsplit Tetra® Elderly Group
Reporting group description:	
Subjects >60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.	

Primary: Anti-HI antibody titers against 4 strains of influenza disease

End point title	Anti-HI antibody titers against 4 strains of influenza disease ^[1]
End point description:	
The strains assessed were: Flu A/Christchurch/16/2010 H1N1 HI, Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata) ,Flu B/Brisbane/60/2008 Victoria HI. Titers are presented as geometric mean titers (GMTs).	
End point type	Primary
End point timeframe:	
At Days 0 and 21	

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Christchurch/16/2010 H1N1, Day 0 [N=60,56]	29.8 (20.7 to 42.8)	14.9 (10.9 to 20.4)		
Flu A/Texas/50/2012 H3N2, Day 0 [N=60,56]	13.1 (10.1 to 17)	13.5 (10.1 to 18.1)		
Flu B/Mass/2/2012 Yamagata, Day 0 [N=60,56]	151 (111.3 to 204.7)	110.4 (88.5 to 137.6)		
Flu B/Brisbane/60/2008 Victoria, Day 0 [N=60,56]	58.5 (44.4 to 77.1)	56.6 (44.6 to 71.7)		
Flu A/Christchurch/16/2010 H1N1, Day 21 [N=60,56]	505 (400.1 to 637.4)	230.3 (160.7 to 330.2)		
Flu A/Texas/50/2012 H3N2, Day 21 [N=60,56]	94 (74.1 to 119.3)	77.9 (58.5 to 103.9)		
Flu B/Mass/2/2012 Yamagata, Day 21 [N=60,56]	792.6 (661.6 to 949.5)	535 (442.2 to 647.2)		
Flu B/Brisbane/60/2008 Victoria, Day 21 [N=60,56]	346.9 (288 to 417.9)	239.2 (193.3 to 296)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against 4 strains of influenza disease

End point title	Number of seroprotected subjects against 4 strains of influenza disease ^[2]
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End point description:

The strains are: Flu A/Christchurch/16/2010 H1N1 HI, Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata), Flu B/Brisbane/60/2008 Victoria HI. A seroprotected subject is defined as a subject with serum HI titre \geq 1:40.

End point type	Primary
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End point timeframe:

At Day 21

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Subjects				
Flu A/Christchurch/16/2010 H1N1, Day 0 [N=60,56]	29	12		
Flu A/Christchurch/16/2010 H1N1, Day 21 [N=60,56]	60	49		
Flu A/Texas/50/2012 H3N2, Day 0 [N=60,56]	12	15		
Flu A/Texas/50/2012 H3N2, Day 21 [N=60,56]	54	40		
Flu B/Mass/2/2012 Yamagata, Day 0 [N=60,56]	56	52		
Flu B/Mass/2/2012 Yamagata, Day 21 [N=60,56]	60	56		
Flu B/Brisbane/60/2008 Victoria, Day 0 [N=60,56]	43	40		
Flu B/Brisbane/60/2008 Victoria, Day 21 [N=60,56]	60	55		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects against 4 strains of influenza disease

End point title	Number of seroconverted subjects against 4 strains of influenza disease ^[3]
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End point description:

The strains are: Flu A/Christchurch/16/2010 H1N1 HI, (referred to as Flu A/Christch/16/2010 H1N1), Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata), Flu B/Brisbane/60/2008 Victoria HI. A seroconverted subject is defined as a subject with either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least 4-fold increase in post-vaccination titer.

End point type	Primary
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End point timeframe:

At Day 21

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Subjects				
Flu A/Christch/16/2010 H1N1, Day 21 [N=60,56]	48	43		
Flu A/Texas/50/2012 H3N2, Day 21 [N=60,56]	41	27		
Flu B/Mass/2/2012 Yamagata, Day 21 [N=60,56]	35	32		
Flu B/Brisbane/60/2008 Victoria, Day 21 [N=60,56]	37	24		

Statistical analyses

No statistical analyses for this end point

Primary: Mean geometric increase (MGI) for HI antibody titer against the 4 flu strains of influenza disease

End point title	Mean geometric increase (MGI) for HI antibody titer against the 4 flu strains of influenza disease ^[4]
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End point description:

The strains are: Flu A/Christchurch/16/2010 H1N1 HI, (referred to as Flu A/Christch/16/2010 H1N1), Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata) Flu B/Brisbane/60/2008 Victoria HI. MGI was defined as the fold increase in serum HI geometric mean titers post-vaccination compared to Day 0.

End point type	Primary
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End point timeframe:

At Day 21

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Fold increase				
geometric mean (confidence interval 95%)				
Flu A/Christch/16/2010 H1N1, Day 21 [N=60,56]	17 (11.6 to 24.8)	15.4 (10.5 to 22.6)		
Flu A/Texas/50/2012 H3N2, Day 21 [N=60,56]	7.2 (5.5 to 9.3)	5.8 (4.3 to 7.8)		
Flu B/Mass/2/2012 Yamagata, Day 21 [N=60,56]	5.3 (3.8 to 7.2)	4.8 (3.9 to 6.1)		
Flu B/Brisbane/60/2008 Victoria, Day 21 [N=60,56]	5.9 (4.4 to 7.9)	4.2 (3.2 to 5.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with seroprotection Powers (SPP) for HI antibody titer against the 4 flu strains of influenza disease

End point title	Number of subjects with seroprotection Powers (SPP) for HI antibody titer against the 4 flu strains of influenza disease ^[5]
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End point description:

The strains are: Flu A/Christchurch/16/2010 H1N1 HI, (referred to as Flu A/Christch/16/2010 H1N1), Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata), Flu B/Brisbane/60/2008 Victoria HI. SPP is defined as the percentage of subjects who had a pre-vaccination titer < 1:40 and a post-vaccination titer ≥ 1:40.

End point type	Primary
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End point timeframe:

During a 4-day follow-up period after vaccination (i.e. day of vaccination and 3 subsequent days)

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	44		
Units: Subjects				
Flu A/Christch/16/2010 H1N1, Day 21 [N=31,44]	31	37		
Flu A/Texas/50/2012 H3N2, Day 21 [N=48,41]	42	25		
Flu B/Mass/2/2012 Yamagata, Day 21 [N=17, 16]	17	15		
Flu B/Brisbane/60/2008 Victoria, Day 21 [N=4,4]	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms
End point description: Assessed solicited local symptoms were ecchymosis, induration, pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 ecchymosis/induration/redness/swelling = ecchymosis/induration/redness/swelling spreading beyond 100 millimeters (mm) of injection site.	
End point type	Secondary
End point timeframe: During a 21-day follow-up period after vaccination (i.e. day of vaccination and 20 subsequent days)	

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Subjects				
Any Ecchymosis	0	0		
Grade 3 Ecchymosis	0	0		
Any Induration	6	5		
Grade 3 Induration	0	0		
Any Pain	37	19		
Grade 3 Pain	1	0		
Any Redness	3	6		
Grade 3 Redness	0	0		
Any Swelling	3	2		
Grade 3 Swelling	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days of solicited local symptoms

End point title	Number of days of solicited local symptoms
End point description: Assessed solicited local symptoms were ecchymosis, induration, pain, redness and swelling. The number of days is expressed as a mean value.	

End point type	Secondary
End point timeframe:	
During the entire study period (Days 0 to 21)	

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	19		
Units: Days				
arithmetic mean (confidence interval 95%)				
Induration [N=6;5]	1.8 (1 to 2)	2.2 (2 to 3)		
Pain [N=37;19]	2.2 (2 to 3)	1.9 (1 to 2)		
Redness [N=3;6]	2 (1 to 3)	1.5 (1 to 2)		
Swelling [N=3;2]	2.7 (2 to 3)	2 (2 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms
End point description:	
Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering, sweating and temperature [defined as oral temperature equal to or above (\geq) 37.5 degrees Celsius ($^{\circ}$ C)],. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever $> 39.0^{\circ}$ C. Related = symptom assessed by the investigator as related to the vaccination.	
End point type	Secondary
End point timeframe:	
During a 4-day follow-up period after vaccination (i.e. day of vaccination and 3 subsequent days)	

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Subjects				
Any Arthralgia	3	6		
Grade 3 Arthralgia	1	0		
Related Arthralgia	1	4		
Any Fatigue	10	4		
Grade 3 Fatigue	1	0		
Related Fatigue	8	2		
Any Gastrointestinal symptoms	3	2		

Grade 3 Gastrointestinal symptoms	0	0		
Related Gastrointestinal symptoms	0	1		
Any Headache	9	5		
Grade 3 Headache	1	0		
Related Headache	4	4		
Any Myalgia	14	7		
Grade 3 Myalgia	1	0		
Related Myalgia	12	5		
Any Sweating	2	0		
Grade 3 Sweating	1	0		
Related Sweating	1	0		
Any Shivering	3	2		
Grade 3 Shivering	1	0		
Related Shivering	3	2		
Any Temperature	0	0		
Grade 3 Temperature	0	0		
Related Temperature	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days of solicited general symptoms

End point title	Number of days of solicited general symptoms
End point description:	
Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering, sweating and temperature [defined as oral temperature equal to or above (\geq) 37.5 degrees Celsius ($^{\circ}$ C)]. Any = occurrence of the symptom regardless of intensity grade. The number of days is expressed as a mean value.	
End point type	Secondary
End point timeframe:	
During a 4-day follow-up period after vaccination (i.e. day of vaccination and 3 subsequent days)	

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: Days				
arithmetic mean (confidence interval 95%)				
Arthralgia [N=3;6]	2.7 (2 to 3)	1.8 (1 to 2)		
Fatigue [N=10;4]	1.6 (1 to 2)	2.8 (2 to 3.5)		
Gastrointestinal symptoms [N=3;2]	2 (1 to 3)	2.5 (1 to 4)		
Headache [N=9;5]	1.9 (1 to 2)	1.4 (1 to 2)		
Myalgia [N=14;7]	1.8 (1 to 2)	2 (1 to 2)		
Sweating [N=3;2]	1.7 (1 to 3)	2 (2 to 2)		
Shivering [N=2;0]	2 (1 to 3)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related unsolicited adverse events (AEs).

End point title	Number of subjects with any, grade 3 and related unsolicited adverse events (AEs).
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End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

During a 4-day follow-up period after vaccination (i.e. day of vaccination and 3 subsequent days)

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Subjects				
Subjects with any AE(s), n (%)	6	9		
Subjects with grade 3 AE(s)	1	0		
Subjects with related AE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related serious adverse events (SAEs).

End point title	Number of subjects with any, grade 3 and related serious adverse events (SAEs).
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End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary
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End point timeframe:

At Days 0 and 21

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Subjects				
Subjects with any SAE(s), n (%)	0	0		
Subjects with related SAE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HI antibody titers against 4 strains of influenza virus by vaccination status

End point title	Anti-HI antibody titers against 4 strains of influenza virus by vaccination status
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End point description:

The strains are: Flu A/Christchurch/16/2010 H1N1 HI, (referred to as Flu A/Christch/16/2010 H1N1), Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata), Flu B/Brisbane/60/2008 Victoria HI. Titers are presented as geometric mean titers (GMTs). Vaccination status is presented as Y = vaccinated or N = not vaccinated during the 2012-2013 season.

End point type	Secondary
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End point timeframe:

At Days 0 and 21

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Christch/16/2010 H1N1, Day 0,Y [N=12,24]	65.4 (31.9 to 134.1)	16.1 (10.5 to 24.7)		
Flu A/Christch/16/2010 H1N1, Day 0,N [N=48,32]	24.5 (16.2 to 36.8)	14.1 (8.9 to 22.4)		
Flu A/Texas/50/2012 H3N2, Day 0, Y [N=12,24]	21.8 (9.5 to 50)	15 (9.4 to 23.8)		
Flu A/Texas/50/2012 H3N2, Day 0, N [N=48,32]	11.5 (8.9 to 15)	12.6 (8.5 to 18.6)		
Flu B/Mass/2/2012 Yamagata, Day 0,Y [N=12,24]	174.4 (88.4 to 343.8)	111.6 (83.7 to 148.7)		

Flu B/Mass/2/2012 Yamagata, Day 0,N [N=48,32]	145.6 (102.4 to 207.1)	109.5 (78.4 to 152.8)		
Flu B/Brisbane/60/2008 Victoria, Day 0,Y [N=12,24]	113.2 (67.2 to 190.8)	62.7 (44.5 to 88.2)		
Flu B/Brisbane/60/2008 Victoria, Day 0,N [N=48,32]	49.6 (36.4 to 67.6)	52.4 (37.2 to 73.6)		
Flu A/Christch/16/2010 H1N1, Day 21,Y [N=12,24]	570.2 (362.2 to 897.4)	198.6 (111.2 to 355)		
Flu A/Christch/16/2010 H1N1, Day 21,N [N=48,32]	489.9 (372.2 to 644.9)	257.4 (159.1 to 416.2)		
Flu A/Texas/50/2012 H3N2, Day 21,Y [N=12,24]	119.9 (67.8 to 211.9)	68.2 (44.9 to 103.7)		
Flu A/Texas/50/2012 H3N2, Day 21,N [N=48,32]	88.5 (67.6 to 115.8)	86.1 (57.3 to 129.6)		
Flu B/Mass/2/2012 Yamagata, Day 21,Y [N=12,24]	522.9 (316.8 to 863)	415.2 (305.8 to 563.6)		
Flu B/Mass/2/2012 Yamagata, Day 21,N [N=48,32]	879.5 (729.8 to 1059.9)	647 (511.9 to 817.8)		
Flu B/Brisbane/60/2008 Victoria,Day 21,Y [N=12,24]	269 (188.1 to 384.8)	162.2 (117.9 to 223.2)		
Flu B/Brisbane/60/2008 Victoria,Day 21,N [N=48,32]	369.7 (297.6 to 459.1)	320 (248.3 to 412.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against 4 strains of influenza virus by vaccination status

End point title	Number of seroprotected subjects against 4 strains of influenza virus by vaccination status
End point description: The strains are: Flu A/Christchurch/16/2010 H1N1 HI, (referred to as Flu A/Christch/16/2010 H1N1), Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata), Flu B/Brisbane/60/2008 Victoria HI. A seroprotected subject is defined as a subject with serum HI titre \geq 1:40. Vaccination status is presented as Y = vaccinated or N = not vaccinated during the 2012-2013 season.	
End point type	Secondary
End point timeframe: At Day 21	

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Subjects				
Flu A/Christch/16/2010 H1N1, Day 0,Y [N=12,24]	9	5		
Flu A/Christch/16/2010 H1N1, Day 0,N [N=48,32]	20	7		
Flu A/Texas/50/2012 H3N2, Day 0, N [N=12,24]	4	7		

Flu A/Texas/50/2012 H3N2, Day 0, N [N=48,32]	8	8		
Flu B/Mass/2/2012 Yamagata, Day 0,Y [N=12,24]	11	23		
Flu B/Mass/2/2012 Yamagata, Day 0,N [N=48,32]	45	29		
Flu B/Brisbane/60/2008 Victoria, Day 0,Y [N=12,24]	11	20		
Flu B/Brisbane/60/2008 Victoria, Day 0,N [N=48,32]	32	20		
Flu A/Christch/16/2010 H1N1, Day 21,Y [N=12,24]	12	21		
Flu A/Christch/16/2010 H1N1, Day 21,N [N=48,32]	48	28		
Flu A/Texas/50/2012 H3N2, Day 21,Y [N=12,24]	11	18		
Flu A/Texas/50/2012 H3N2, Day 21,N [N=48,32]	43	22		
Flu B/Mass/2/2012 Yamagata, Day 21,Y [N=12,24]	12	24		
Flu B/Mass/2/2012 Yamagata, Day 21,N [N=48,32]	48	32		
Flu B/Brisbane/60/2008 Victoria,Day 21,Y [N=12,24]	12	23		
Flu B/Brisbane/60/2008 Victoria,Day 21,N [N=48,32]	48	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against 4 strains of influenza virus by vaccination status

End point title	Number of seroconverted subjects against 4 strains of influenza virus by vaccination status
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End point description:

The strains are: Flu A/Christchurch/16/2010 H1N1 HI, (referred to as Flu A/Christch/16/2010 H1N1), Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata), Flu B/Brisbane/60/2008 Victoria HI. A seroconverted subject is defined as a subject with either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least 4-fold increase in post-vaccination titer. Vaccination status is presented as Y = vaccinated or N = not vaccinated during the 2012-2013 season.

End point type	Secondary
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End point timeframe:

At Day 21

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Subjects				

Flu A/Christch/16/2010 H1N1, Day 21,Y [N=12,24]	8	18		
Flu A/Christch/16/2010 H1N1, Day 21,N [N=60,57]	40	25		
Flu A/Texas/50/2012 H3N2, Day 21,Y [N=12,24]	7	10		
Flu A/Texas/50/2012 H3N2, Day 21,N [N=60,57]	34	17		
Flu B/Mass/2/2012 Yamagata, Day 21,Y [N=12,24]	3	10		
Flu B/Mass/2/2012 Yamagata, Day 21,N [N=60,57]	32	22		
Flu B/Brisbane/60/2008 Victoria,Day 21,Y [N=12,24]	2	4		
Flu B/Brisbane/60/2008 Victoria,Day 21,N [N=60,57]	35	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean geometric increase (MGI) for HI antibody titer against the 4 flu strains of influenza virus by vaccination status

End point title	Mean geometric increase (MGI) for HI antibody titer against the 4 flu strains of influenza virus by vaccination status
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End point description:

The strains are: Flu A/Christchurch/16/2010 H1N1 HI, (referred to as Flu A/Christch/16/2010 H1N1), Flu A/Texas/50/2012 H3N2 HI, Flu B/Massachusetts/2/2012 Yamagata HI, (referred to as Flu B/Mass/2/2012 Yamagata), Flu B/Brisbane/60/2008 Victoria HI. MGI was defined as the fold increase in serum HI geometric mean titers post-vaccination compared to Day 0. Vaccination status is presented as Y = vaccinated or N = not vaccinated during the 2012-2013 season.

End point type	Secondary
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End point timeframe:

At Day 21

End point values	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	56		
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/Christch/16/2010 H1N1, Day 21,Y [N=12,24]	8.7 (3.3 to 23.2)	12.4 (7.1 to 21.6)		
Flu A/Christch/16/2010 H1N1, Day 21,N [N=48,32]	20 (13.2 to 30.3)	18.2 (10.6 to 31.4)		
Flu A/Texas/50/2012 H3N2, Day 21,Y [N=12,24]	5.5 (2.5 to 12)	4.6 (2.9 to 7.2)		
Flu A/Texas/50/2012 H3N2, Day 21,N [N=48,32]	7.7 (5.8 to 10.1)	6.9 (4.5 to 10.4)		
Flu B/Mass/2/2012 Yamagata, Day 21,Y [N=12,24]	3 (1.6 to 5.7)	3.7 (2.7 to 5.2)		

Flu B/Mass/2/2012 Yamagata, Day 21,N [N=48,32]	6 (4.2 to 8.6)	5.9 (4.4 to 7.9)		
Flu B/Brisbane/60/2008 Victoria,Day 21,Y [N=12,24]	2.4 (1.6 to 3.6)	2.6 (1.7 to 3.9)		
Flu B/Brisbane/60/2008 Victoria,Day 21,N [N=48,32]	7.4 (5.4 to 10.3)	6.1 (4.2 to 8.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: Days 0-4 post-vaccination, unsolicited AEs: days 0-21 post-vaccination, SAEs: the entire study duration (Days 0-21 post-vaccination).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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Reporting groups

Reporting group title	Fluarix/Influsplit Tetra® Adult Group
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Reporting group description:

Subjects 18-60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.

Reporting group title	Fluarix/Influsplit Tetra® Elderly Group
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Reporting group description:

Subjects >60 years of age receiving Fluarix/Influsplit Tetra® 2013-2014, administered intramuscularly in the deltoid region of the non-dominant arm.

Serious adverse events	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	0 / 57 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Fluarix/Influsplit Tetra® Adult Group	Fluarix/Influsplit Tetra® Elderly Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 60 (61.67%)	19 / 57 (33.33%)	
General disorders and administration site conditions			
Induration			
subjects affected / exposed	6 / 60 (10.00%)	5 / 57 (8.77%)	
occurrences (all)	6	5	
Pain			
subjects affected / exposed	37 / 60 (61.67%)	19 / 57 (33.33%)	
occurrences (all)	37	19	

Redness			
subjects affected / exposed	3 / 60 (5.00%)	6 / 57 (10.53%)	
occurrences (all)	3	6	
Swelling			
subjects affected / exposed	3 / 60 (5.00%)	2 / 57 (3.51%)	
occurrences (all)	3	2	
Arthralgia			
subjects affected / exposed	3 / 60 (5.00%)	6 / 57 (10.53%)	
occurrences (all)	3	6	
Fatigue			
subjects affected / exposed	10 / 60 (16.67%)	4 / 57 (7.02%)	
occurrences (all)	10	4	
Gastrointestinal symptoms			
subjects affected / exposed	3 / 60 (5.00%)	2 / 57 (3.51%)	
occurrences (all)	3	2	
Headache			
subjects affected / exposed	9 / 60 (15.00%)	5 / 57 (8.77%)	
occurrences (all)	9	5	
Myalgia			
subjects affected / exposed	14 / 60 (23.33%)	7 / 57 (12.28%)	
occurrences (all)	14	7	
Sweating			
subjects affected / exposed	3 / 60 (5.00%)	2 / 57 (3.51%)	
occurrences (all)	3	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported