



Clinical trial results:

A Phase III, open-label, non-randomised, multi-centre, single dose study to assess immunogenicity and safety of Fluarix / Influsplit SSW 2013/2014 injected intramuscularly in adults (18 to 60 years of age) and in the elderly (over 60 years of age)

Summary

EudraCT number	2013-000855-42
Trial protocol	DE
Global end of trial date	02 August 2013

Results information

Result version number	v2
This version publication date	28 May 2016
First version publication date	19 March 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Typos/information were corrected in endpoint description for 1 primary endpoint (GMT) and in the reporting groups for the secondary endpoints.

Trial information

Trial identification

Sponsor protocol code	200160
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01884519
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	09 August 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 August 2013
Global end of trial reached?	Yes
Global end of trial date	02 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 SSW 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	12 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: 120
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	120
From 65 to 84 years	0

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 18-60 Years Group

Arm description:

Subjects 18-60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.

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

Dosage and administration details:

Subjects 18-60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.

Arm title	Fluarix/Influsplit > 60 Years Group
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Arm description:

Subjects above 60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.

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

Dosage and administration details:

Subjects above 60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.

Number of subjects in period 1	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group
Started	60	60
Completed	60	60

Baseline characteristics

Reporting groups

Reporting group title	Fluarix/Influsplit 18-60 Years Group
Reporting group description:	
Subjects 18-60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.	
Reporting group title	Fluarix/Influsplit > 60 Years Group
Reporting group description:	
Subjects above 60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.	

Reporting group values	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group	Total
Number of subjects	60	60	120
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	60	60	120
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
geometric mean	42.6	68.2	
standard deviation	± 11.5	± 5.49	-
Gender categorical			
Units: Subjects			
Female	38	34	72
Male	22	26	48

End points

End points reporting groups

Reporting group title	Fluarix/Influsplit 18-60 Years Group
Reporting group description: Subjects 18-60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.	
Reporting group title	Fluarix/Influsplit > 60 Years Group
Reporting group description: Subjects above 60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.	
Subject analysis set title	Fluarix/Influsplit > 60 Years Group with Vaccination
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects aged >60 years of age receiving Fluarix/Influsplit SSW 2013-2014	
Subject analysis set title	Fluarix/Influsplit > 60 Years Group without Vaccination
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects aged >60 years of age not receiving Fluarix/Influsplit SSW 2013-2014	
Subject analysis set title	Fluarix/Influsplit 18-60 years Group with Vaccination
Subject analysis set type	Sub-group analysis
Subject analysis set description: Fluarix/Influsplit 18-60 years Group with Vaccination: Subjects 18-60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0 and who had received an influenza vaccine during the 2 influenza seasonal prior to season 2012-2013. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.	
Subject analysis set title	Fluarix/Influsplit 18-60 years Group without Vaccination
Subject analysis set type	Sub-group analysis
Subject analysis set description: Fluarix/Influsplit 18-60 years Group without Vaccination: Subjects 18-60 years of age received 1 dose of Fluarix/Influsplit SSW 2013-2014 vaccine at Day 0 and who had not received an influenza vaccine during the 2 influenza seasonal prior to season 2012-2013. The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.	

Primary: Humoral immune response in terms of Haemagglutination Inhibition (HI) antibody titers against each of the three vaccine influenza strains

End point title	Humoral immune response in terms of Haemagglutination Inhibition (HI) antibody titers against each of the three vaccine influenza strains ^[1]
End point description: HI Antibody titers were expressed as Geometric mean titers (GMTs). The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata).	
End point type	Primary
End point timeframe: At Day 0 and Day 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 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Titer				
geometric mean (confidence interval 95%)				
H1N1, Day 0	27.3 (20.3 to 36.8)	15.7 (12.1 to 20.4)		
H1N1, Day 21	444.6 (335.6 to 588.9)	197 (142.6 to 272.1)		
H3N2, Day 0	15.8 (11.9 to 21.1)	14.2 (11 to 18.4)		
H3N2, Day 21	73.8 (57.8 to 94.2)	80 (58.4 to 109.5)		
Yamagata, Day 0	105 (83.6 to 131.8)	95.2 (77.5 to 116.9)		
Yamagata, Day 21	424.6 (347.6 to 518.8)	327.5 (266.2 to 402.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects who were seroprotected for anti-HI antibodies against each of the three vaccine influenza strains.

End point title	Number of subjects who were seroprotected for anti-HI antibodies against each of the three vaccine influenza strains. ^[2]
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End point description:

A seroprotected subject was defined as a vaccinated subject. The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata).

End point type	Primary
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End point timeframe:

At Day 0 and 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 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
H1N1, Day 0	25	14		
H1N1, Day 21	58	56		
H3N2, Day 0	12	12		
H3N2, Day 21	50	44		
Yamagata, Day 0	53	55		
Yamagata, Day 21	60	60		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects for anti-HIA antibodies against each of the three vaccine influenza strains.

End point title	Number of seroconverted subjects for anti-HIA antibodies against each of the three vaccine influenza strains. ^[3]
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End point description:

A seroconverted subjects was defined as a vaccinated subject with either a pre-vaccination titer less than (<) 1:10 and a post-vaccination titer \geq 1:40, or a pre-vaccination titer \geq 1:10 and at least a 4-fold increase in post-vaccination titer. The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata).

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 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
H1N1	44	46		
H3N2	31	29		
Yamagata	30	23		

Statistical analyses

No statistical analyses for this end point

Primary: Mean geometric increase (MG I) for haemagglutination inhibition (HI) antibody titer against each of the three vaccine influenza strains.

End point title	Mean geometric increase (MG I) for haemagglutination inhibition (HI) antibody titer against each of the three vaccine influenza strains. ^[4]
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End point description:

MG I was defined as the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination (Day 0). The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata).

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 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Fold increase				
geometric mean (confidence interval 95%)				
H1N1	16.3 (10.8 to 24.5)	12.6 (8.7 to 18.2)		
H3N2	4.7 (3.4 to 6.4)	5.6 (4 to 7.9)		
Yamagata	4 (3.1 to 5.3)	3.4 (2.7 to 4.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with seroprotection power (SPP) for HI antibody titer against each of the three vaccine Influenza strains above the cut-off value.

End point title	Number of subjects with seroprotection power (SPP) for HI antibody titer against each of the three vaccine Influenza strains above the cut-off value. ^[5]
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End point description:

SPP was defined as the number of vaccinated subjects with a pre-vaccination titer < 1:40 and a post-vaccination titer ≥ 1:40. The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata).

End point type	Primary
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End point timeframe:

At Day 21

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 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	48		
Units: Subjects				
H1N1 [N=35,46]	33	42		
H3N2 [N=48,48]	38	32		
Yamagata [N=7,5]	7	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Humoral immune response in terms of HI antibody titers against each of the three vaccine influenza strains

End point title	Humoral immune response in terms of HI antibody titers against each of the three vaccine influenza strains
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End point description:

HI antibody titers were expressed as Geometric mean titers (GMTs). The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata). This outcome measure was assessed by influenza vaccination status in subjects (18-60 years and >60 years) who had and who had not received an influenza vaccine during the 2 influenza seasons prior to season 2012/2013.

End point type	Secondary
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End point timeframe:

At Days 0 and 21

End point values	Fluarix/Influsplit > 60 Years Group with Vaccination	Fluarix/Influsplit > 60 Years Group without Vaccination	Fluarix/Influsplit 18-60 years Group with Vaccination	Fluarix/Influsplit 18-60 years Group without Vaccination
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	31	20	40
Units: Titer				
geometric mean (confidence interval 95%)				
H1N1, Day 0	16.3 (10.5 to 25.2)	15.1 (10.9 to 21)	28.7 (17.2 to 48.1)	26.6 (18.2 to 38.9)
H1N1, Day 21	158.2 (99.1 to 252.5)	241.9 (152.7 to 383.3)	348.8 (200.3 to 607.4)	501.9 (361 to 698)
H3N2, Day 0	17.3 (11.4 to 26.2)	11.8 (8.6 to 16.2)	18.6 (10.8 to 32)	14.6 (10.3 to 20.8)
H3N2, Day 21	58.6 (39.9 to 86.2)	106.9 (65.6 to 174.3)	60.6 (39.3 to 93.5)	81.4 (60 to 110.4)
Yamagata, Day 0	110.6 (84.6 to 144.5)	82.7 (60.3 to 113.4)	109.3 (74.3 to 160.9)	102.9 (76.7 to 138)
Yamagata, Day 21	237.3 (184.2 to 305.8)	442.6 (328.9 to 595.7)	355 (247.3 to 509.5)	464.4 (362.9 to 594.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who were seroprotected for anti-HI antibodies against each of the three vaccine influenza strains.

End point title	Number of subjects who were seroprotected for anti-HI antibodies against each of the three vaccine influenza strains.
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End point description:

A seroprotected subject was defined as the number of a vaccinated subjects with a serum HI titer greater than or equal to (\geq) 1:40 that usually is accepted as indicating protection in adults. The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata). This outcome measure was assessed by influenza vaccination status in subjects (18-60 years and >60 years) who had and who had not received an influenza vaccine during the 2 influenza seasons prior to season 2012/2013.

End point type	Secondary
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End point timeframe:

At Day 0 and Day 21

End point values	Fluarix/Influsplit > 60 Years Group with Vaccination	Fluarix/Influsplit > 60 Years Group without Vaccination	Fluarix/Influsplit 18-60 years Group with Vaccination	Fluarix/Influsplit 18-60 years Group without Vaccination
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	31	20	40
Units: Subjects				
H1N1, Day 0	8	6	9	16
H1N1, Day 21	26	30	19	39
H3N2, Day 0	6	6	5	7
H3N2, Day 21	20	24	16	34
Yamagata, Day 0	29	26	18	35
Yamagata, Day 21	29	31	20	40

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for anti-HA antibodies against each of the three vaccine influenza strains.

End point title	Number of seroconverted subjects for anti-HA antibodies against each of the three vaccine influenza strains.
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End point description:

A seroconverted subjects was defined as a vaccinated subjects with either a pre-vaccination titer less than ($<$) 1:10 and a post-vaccination titer \geq 1:40, or a pre-vaccination titer \geq 1:10 and at least a 4-fold increase in post-vaccination titer. The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata). This outcome measure was assessed by influenza vaccination status in subjects (18-60 years and >60 years) who had and who had not received an influenza vaccine during the 2 influenza seasons prior to season 2012/2013.

End point type	Secondary
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End point timeframe:

At Day 21

End point values	Fluarix/Influsplit > 60 Years Group with Vaccination	Fluarix/Influsplit > 60 Years Group without Vaccination	Fluarix/Influsplit 18-60 years Group with Vaccination	Fluarix/Influsplit 18-60 years Group without Vaccination
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	31	20	40
Units: Subjects				
H1N1	20	26	13	31
H3N2	10	19	8	23
Yamagata	5	18	6	24

Statistical analyses

No statistical analyses for this end point

Secondary: Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibody titer against each of the three vaccine influenza strains.

End point title	Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibody titer against each of the three vaccine influenza strains.
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End point description:

MGI was defined as the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination (Day 0). The vaccine strains assessed were Flu A/Christchurch/16/2010 (H1N1), Flu A/Texas/50/2012 (H3N2) and Flu B/Massachusetts/2/2012 (Yamagata). This outcome measure was assessed by influenza vaccination status in subjects (18-60 years and >60 years) who had and who had not received an influenza vaccine during the 2 influenza seasons prior to season 2012/2013.

End point type	Secondary
End point timeframe:	
At Day 21	

End point values	Fluarix/Influsplit > 60 Years Group with Vaccination	Fluarix/Influsplit > 60 Years Group without Vaccination	Fluarix/Influsplit 18-60 years Group with Vaccination	Fluarix/Influsplit 18-60 years Group without Vaccination
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	31	20	40
Units: Fold increase				
geometric mean (confidence interval 95%)				
H1N1	9.7 (5.5 to 17)	16 (9.7 to 26.5)	12.1 (5.8 to 25.4)	18.9 (11.4 to 31.4)
H3N2	3.4 (2.4 to 4.8)	9.1 (5.3 to 15.5)	3.3 (2 to 5.2)	5.6 (3.7 to 8.3)
Yamagata	2.1 (1.7 to 2.7)	5.4 (3.9 to 7.4)	3.2 (2 to 5.2)	4.5 (3.2 to 6.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms.

End point title	Number of subjects reporting any and grade 3 solicited local symptoms.
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End point description:

Solicited local symptoms assessed were ecchymosis, induration, pain, redness and swelling. Any was defined as any solicited local symptom reported irrespective of intensity. Grade 3 pain was defined as pain that prevented normal everyday activities. Grade 3 ecchymosis, induration, redness and swelling was greater than 100 millimeters (mm) i.e. >100mm.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any Ecchymosis	0	0		
Grade 3 Ecchymosis	0	0		
Any Induration	0	2		
Grade 3 Induration	0	0		
Any Pain	38	15		
Grade 3 Pain	0	0		
Any Redness	8	3		
Grade 3 Redness	0	0		
Any Swelling	6	2		
Grade 3 Swelling	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of solicited local symptoms.

End point title	Duration of solicited local symptoms.
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End point description:

Duration was defined as number of days with any grade of local symptoms.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	15		
Units: Days				
median (full range (min-max))				
Induration [N=0,2]	0 (0 to 0)	1.5 (1 to 2)		
Pain [N=38, 15]	2 (1 to 4)	2 (1 to 4)		
Redness [N=8,3]	2 (1 to 4)	2 (2 to 4)		
Swelling [N=6,2]	1 (1 to 4)	2 (2 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms.

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms.
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End point description:

Solicited general symptoms assessed were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering, increased sweating and fever [axillary temperature above 37.5 degrees Celsius (°C)]. Gastrointestinal symptoms included nausea, vomiting, diarrhea and/or abdominal pain. Any = any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related = symptoms considered by the investigator to have a causal relationship to vaccination. Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 fever = axillary temperature above 39.0°C

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any Arthralgia	5	5		
Grade 3 Arthralgia	0	0		
Related Arthralgia	4	3		
Any Fatigue	10	7		
Grade 3 Fatigue	0	0		
Related Fatigue	6	4		
Any Gastrointestinal symptoms	4	1		
Grade 3 Gastrointestinal symptoms	0	0		
Related Gastrointestinal symptoms	3	1		
Any Headache	10	5		
Grade 3 Headache	2	0		
Related Headache	9	5		

Any Myalgia	14	5		
Grade 3 Myalgia	0	0		
Related Myalgia	12	4		
Any Shivering	4	0		
Grade 3 Shivering	0	0		
Related Shivering	4	0		
Any Sweating	3	7		
Grade 3 Sweating	0	0		
Related Sweating	1	4		
Any Fever ($\geq 37.5^{\circ}\text{C}$)	0	1		
Grade 3 Fever ($> 39.0^{\circ}\text{C}$)	0	0		
Related Fever	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of solicited general symptoms.

End point title	Duration of solicited general symptoms.
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End point description:

Duration was defined as number of days with any grade of general symptoms.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: Days				
median (full range (min-max))				
Arthralgia [N=5,5]	1 (1 to 4)	1 (1 to 4)		
Fatigue [N=10, 7]	1 (1 to 2)	2 (1 to 4)		
Gastrointestinal symptoms [N=4,1]	1 (1 to 1)	3 (3 to 3)		
Headache [N=10,5]	1.5 (1 to 3)	1 (1 to 2)		
Myalgia [N=14,5]	1 (1 to 4)	2 (1 to 3)		
Sweating [N=3,7]	1 (1 to 1)	1 (1 to 4)		
Shivering [N=4,0]	1 (1 to 1)	0 (0 to 0)		
Fever (Axillary) [N=0,1]	0 (0 to 0)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

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

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

Unsolicited AE covers any AE 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 occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination. Grade 3 was an event that prevented normal activities and related was defined as an unsolicited AE assessed by the investigator to be causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

During the 21-day (Days 0-20) post-vaccination period

End point values	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any Unsolicited AEs	5	3		
Grade 3 Unsolicited AEs	0	0		
Related Unsolicited AEs	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and related serious adverse events (SAEs)

End point title	Number of subjects reporting any and related serious adverse events (SAEs)
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End point description:

A serious adverse event was any untoward medical occurrence that: resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

During the entire study period (Days 0-180)

End point values	Fluarix/Influsplit 18-60 Years Group	Fluarix/Influsplit > 60 Years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any SAEs	0	0		
Related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events: From Day 0 to Day 180; Solicited local and general symptoms: During the 4-day (Days 0-3) post-vaccination period; Unsolicited symptoms: During the 21-day (Day 0-20) post-vaccination period

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, the number of participants at risk included those from Total Vaccinated Cohort who had the symptom sheet completed.

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 > 60 Years Group
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Reporting group description: -

Reporting group title	Fluarix/Influsplit 18-60 Years Group
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Reporting group description: -

Serious adverse events	Fluarix/Influsplit > 60 Years Group	Fluarix/Influsplit 18-60 Years Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (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 > 60 Years Group	Fluarix/Influsplit 18-60 Years Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 60 (41.67%)	38 / 60 (63.33%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	15 / 60 (25.00%)	38 / 60 (63.33%)	
occurrences (all)	15	38	
Redness			
subjects affected / exposed	3 / 60 (5.00%)	8 / 60 (13.33%)	
occurrences (all)	3	8	
Swelling			

subjects affected / exposed	2 / 60 (3.33%)	6 / 60 (10.00%)	
occurrences (all)	2	6	
Arthralgia			
subjects affected / exposed	5 / 60 (8.33%)	5 / 60 (8.33%)	
occurrences (all)	5	5	
Fatigue			
subjects affected / exposed	7 / 60 (11.67%)	10 / 60 (16.67%)	
occurrences (all)	7	10	
Gastrointestinal symptoms			
subjects affected / exposed	1 / 60 (1.67%)	4 / 60 (6.67%)	
occurrences (all)	1	4	
Headache			
subjects affected / exposed	5 / 60 (8.33%)	10 / 60 (16.67%)	
occurrences (all)	5	10	
Myalgia			
subjects affected / exposed	5 / 60 (8.33%)	14 / 60 (23.33%)	
occurrences (all)	5	14	
Shivering			
subjects affected / exposed	0 / 60 (0.00%)	4 / 60 (6.67%)	
occurrences (all)	0	4	
Sweating			
subjects affected / exposed	7 / 60 (11.67%)	3 / 60 (5.00%)	
occurrences (all)	7	3	

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