Clinical trial results:
An open, phase IV study on the immunogenicity and tolerability of Influsplit SSW® 2005/2006 in children aged 6-13 years.

Summary

EudraCT number	2005-004517-14
Trial protocol	DE
Global end of trial date	28 March 2006

Results information

Result version number	v1 (current)
This version publication date	13 December 2018
First version publication date	13 December 2018

Trial information

Trial identification

Sponsor protocol code	106252

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00372255
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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?	Yes
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	31 October 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 March 2006
Global end of trial reached?	Yes
Global end of trial date	28 March 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Descriptive analysis of the humoral immune response after one or two dose intramuscular administration of a trivalent influenza split vaccine 2005/2006 in children from 6 years to 9 years measured by the geometric mean titers (GMTs) of the haemagglutination-inhibition antibodies against the three influenza virus strains represented in the vaccine and measured by the seroconversion rates

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2005
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: 224
Worldwide total number of subjects	224
EEA total number of subjects	224

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)	110
Adolescents (12-17 years)	114
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted by a principal investigator and 22 investigators in 18 centers in Germany.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	224
Number of subjects completed	224

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	Influsplit SSW 2005/2006 6-9 years Group

Arm description:

Subjects aged 6 to 9 years who received 2 doses of Influsplit SSW 2005/2006 vaccine at an interval of 4 weeks (Day 0 and Day 28 ± 2).

Arm type	Experimental
Investigational medicinal product name	Influsplit SSW 2005/2006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Children received 2 doses of Influsplit vaccine in the non-dominant arm

Arm title	Influsplit SSW 2005/2006 10-13 years Group

Arm description:

Subjects aged 10 to 13 years who received 1 dose of Influsplit SSW 2005/2006 vaccine at Day 0.

Arm type	Active comparator
Investigational medicinal product name	Influsplit SSW 2005/2006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Children received 1 dose of Influsplit vaccine in the non-dominant.

Number of subjects in period 1	Influsplit SSW 2005/2006 6-9 years Group	Influsplit SSW 2005/2006 10-13 years Group
Started	110	114
Completed	108	113
Not completed	2	1
Lost to follow-up	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Influsplit SSW 2005/2006 6-9 years Group
Reporting group description:	
Subjects aged 6 to 9 years who received 2 doses of Influsplit SSW 2005/2006 vaccine at an interval of 4 weeks (Day 0 and Day 28 ± 2).	
Reporting group title	Influsplit SSW 2005/2006 10-13 years Group
Reporting group description:	
Subjects aged 10 to 13 years who received 1 dose of Influsplit SSW 2005/2006 vaccine at Day 0.	

Reporting group values	Influsplit SSW 2005/2006 6-9 years Group	Influsplit SSW 2005/2006 10-13 years Group	Total
Number of subjects	110	114	224
Age categorical Units: Subjects			
Number of subjects	110	114	224
Age continuous Units: years			
arithmetic mean	7.4	11.3	
standard deviation	± 1.13	± 1.07	-
Gender categorical Units: Subjects			
Female	62	65	127
Male	48	49	97
Race/Ethnicity, Customized Units: Subjects			
White/Caucasian	107	111	218
Not Specified	3	3	6

End points

End points reporting groups

Reporting group title	Influsplit SSW 2005/2006 6-9 years Group
Reporting group description:	
Subjects aged 6 to 9 years who received 2 doses of Influsplit SSW 2005/2006 vaccine at an interval of 4 weeks (Day 0 and Day 28 ± 2).	
Reporting group title	Influsplit SSW 2005/2006 10-13 years Group
Reporting group description:	
Subjects aged 10 to 13 years who received 1 dose of Influsplit SSW 2005/2006 vaccine at Day 0.	

Primary: Titers for serum Hemagglutination Inhibition (HI) antibodies against 3 strains of influenza disease in children aged between 6 and 9 years

End point title	Titers for serum Hemagglutination Inhibition (HI) antibodies against 3 strains of influenza disease in children aged between 6 and 9 years[1][2]
End point description:	
Titers of serum HI antibodies are presented as geometric mean titers (GMTs) against the three influenza strains contained in the trivalent influenza vaccine Influsplit SSW 2005/2006 (GlaxoSmithKline/SSW) after a single versus after two vaccine doses of Influsplit SSW 2005/2006. The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.	
End point type	Primary
End point timeframe:	
28 days after Dose 1 (Day 28) and 21 days after Dose 2 (Day 49 ± 2)	

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 scope of this endpoint was descriptive analysis. No statistical analyses were performed.
[2] - 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: This analysis was performed only on subjects belonging to the specific age group- 6 to 9 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 6-9 years Group			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Titer				
geometric mean (confidence interval 95%)				
A/New Caledonia (H1N1), Dose 1(N-97)	290.4 (165.6 to 509.3)			
A/New Caledonia (H1N1), Dose 2 (N-95)	719.2 (503.3 to 1027.7)			
A/New York (H3N2), Dose 1(N-97)	381.2 (281.3 to 516.6)			
A/New York (H3N2), Dose 2 (N-95)	393.9 (313.5 to 494.9)			
B/Jiangsu, Dose 1(N-97)	97.7 (68.6 to 139.2)			
B/Jiangsu, Dose 2 (N-95)	301.8 (246.3 to 369.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Seroconversion factor (SCF) for HI antibodies against 3 strains of influenza disease in children aged between 6 and 9 years

End point title	Seroconversion factor (SCF) for HI antibodies against 3 strains of influenza disease in children aged between 6 and 9 years[3][4]

End point description:

Seroconversion factors were defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0. The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.

End point type	Primary

End point timeframe:

28 days after Dose 1 (Day 28) and 21 days after Dose 2 (Day 49 ± 2)

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 scope of this endpoint was descriptive analysis. No statistical analyses were performed.
[4] - 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: This analysis was performed only on subjects belonging to the specific age group- 6 to 9 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 6-9 years Group			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Fold increase				
geometric mean (confidence interval 95%)				
A/New Caledonia (H1N1), Dose 1(N-97)	16.7 (11.8 to 23.8)			
A/New Caledonia (H1N1), Dose 2 (N-95)	40.7 (32.6 to 50.8)			
A/New York (H3N2), Dose 1(N-97)	14.9 (10.9 to 20.3)			
A/New York (H3N2), Dose 2 (N-95)	15.4 (11.9 to 20.0)			
B/Jiangsu, Dose 1(N-97)	8.5 (6.7 to 10.7)			
B/Jiangsu, Dose 2 (N-95)	26.1 (21.4 to 31.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects against 3 strains of influenza disease in children aged between 6 and 9 years

End point title	Number of seroconverted subjects against 3 strains of influenza disease in children aged between 6 and 9 years[5][6]

End point description:

A seroconverted subject was defined as a subject who was either seronegative prior to the vaccination and had a protective post-vaccination titer of greater than or equal to (≥) 1:40 or who was seropositive prior to the vaccination and had at least a 4-fold increase in the titer as the outcome of the vaccination. The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.

End point type	Primary

End point timeframe:

28 days after Dose 1 (Day 28) and 21 days after Dose 2 (Day 49 ± 2)

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 scope of this endpoint was descriptive analysis. No statistical analyses were performed.
[6] - 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: This analysis was performed only on subjects belonging to the specific age group- 6 to 9 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 6-9 years Group			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Participants				
A/New Caledonia (H1N1), Dose 1(N-97)	63			
A/New Caledonia (H1N1), Dose 2 (N-95)	93			
A/New York (H3N2), Dose 1(N-97)	79			
A/New York (H3N2), Dose 2 (N-95)	80			
B/Jiangsu, Dose 1(N-97)	66			
B/Jiangsu, Dose 2 (N-95)	92			

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for serum HI antibodies against 3 strains of influenza disease in children aged between 10 and 13 years

End point title	Titers for serum HI antibodies against 3 strains of influenza disease in children aged between 10 and 13 years[7]

End point description:

Titers of serum HI antibodies are presented as geometric mean titers (GMTs) against the three influenza strains contained in the trivalent influenza vaccine Influsplit SSW 2005/2006 (GlaxoSmithKline/SSW) after a single versus after two vaccine doses of Influsplit SSW 2005/2006. The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.

End point type	Secondary

End point timeframe:

21 days post-vaccination (Day 21)

Notes:

[7] - 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: This analysis was performed only on subjects belonging to the specific age group- 10 to 13 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 10-13 years Group			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Titers				
geometric mean (confidence interval 95%)				
A/New Caledonia (H1N1), Dose 1 (N-106)	1326.6 (856.7 to 2054.3)			
A/New York (H3N2), Dose 1(N-106)	300.6 (241.5 to 374.2)			
B/Jiangsu, Dose 1(N-106)	218.9 (169.1 to 283.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: SCF for HI antibodies against 3 strains of influenza disease in children aged between 10 and 13 years

End point title	SCF for HI antibodies against 3 strains of influenza disease in children aged between 10 and 13 years[8]

End point description:

Seroconversion factors were defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.

End point type	Secondary

End point timeframe:

21 days post-vaccination (Day 21)

Notes:

[8] - 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: This analysis was performed only on subjects belonging to the specific age group- 10 to 13 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 10-13 years Group			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Fold increase				
geometric mean (confidence interval 95%)				
A/New Caledonia (H1N1), Dose 1(N-106)	50.2 (36.2 to 69.8)			
A/New York (H3N2), Dose 1(N-106)	10.3 (8.2 to 12.8)			
B/Jiangsu, Dose 1(N-106)	12.6 (10.4 to 15.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against 3 strains of influenza disease in children aged between 10 and 13 years

End point title	Number of seroconverted subjects against 3 strains of influenza disease in children aged between 10 and 13 years[9]

End point description:

A seroconverted subject was defined as a subject who was either seronegative prior to the vaccination and had a protective post-vaccination titer of greater than or equal to (≥) 1:40 or who was seropositive prior to the vaccination and had at least a 4-fold increase in the titer as the outcome of the vaccination. The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.

End point type	Secondary

End point timeframe:

21 days post-vaccination (Day 21)

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: This analysis was performed only on subjects belonging to the specific age group- 10 to 13 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 10-13 years Group			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Participants				
A/New Caledonia (H1N1), Dose 1(N-106)	90			
A/New York (H3N2), Dose 1(N-106)	83			
B/Jiangsu, Dose 1(N-106)	90			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects who were unprotected at pre-vaccination against 3 influenza strains in children aged between 10 and 13 years

End point title	Number of seroprotected subjects who were unprotected at pre-vaccination against 3 influenza strains in children aged between 10 and 13 years[10]

End point description:

Seroprotection power (SPP) was defined as the proportion of the subjects unprotected before vaccination (titre < 40) who were protected after vaccination (titer ≥ 40). The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.

End point type	Secondary

End point timeframe:

21 days post-vaccination (Day 21)

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: This analysis was performed only on subjects belonging to the specific age group- 10 to 13 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 10-13 years Group			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Participants				
A/New Caledonia (H1N1), Dose 1 (N-48)	33			
A/New York (H3N2), Dose 1 (N-57)	52			
B/Jiangsu, Dose 1 (N-75)	62			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against 3 strains of influenza disease in children aged between 10 and 13 years

End point title	Number of seroprotected subjects against 3 strains of influenza disease in children aged between 10 and 13 years[11]

End point description:

A seroprotected subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer ≥ 1:40. The three influenza strains assessed were: A/New Caledonia (H1N1), A/New York (H3N2), B/Jiangsu.

End point type	Secondary

End point timeframe:

21 days post-vaccination (Day 21)

Notes:

[11] - 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: This analysis was performed only on subjects belonging to the specific age group- 10 to 13 years. Therefore, data are not presented for the other group.

End point values	Influsplit SSW 2005/2006 10-13 years Group			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Participants				
A/New Caledonia (H1N1), Dose 1 (N-106)	91			
A/New York (H3N2), Dose 1 (N-106)	101			
B/Jiangsu, Dose 1(N-106)	93			

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 pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 50 millimeters (mm) of injection site.

End point type	Secondary

End point timeframe:

During the 4-day (Day 0–3) post-vaccination period following each dose and across doses

End point values	Influsplit SSW 2005/2006 6-9 years Group	Influsplit SSW 2005/2006 10-13 years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	114		
Units: Participants				
Pain, Any, Dose 1 (N-110,114)	62	54		
Pain, Grade 3, Dose 1 (N-110,114)	0	1		
Redness, Any, Dose 1 (N-110,114)	28	24		
Redness, > 50 mm, Dose 1 (N-110,114)	0	0		
Swelling, Any, Dose 1 (N-110,114)	28	39		
Swelling, > 50 mm, Dose 1 (N-110,114)	0	0		
Pain, Any, Dose 2 (N-108,0)	68	0		
Pain, Grade 3, Dose 2 (N-108,0)	1	0		
Redness, Any, Dose 2(N-108,0)	31	0		
Redness, > 50 mm, Dose 2(N-108,0)	0	0		
Swelling, Any, Dose 2(N-108,0)	35	0		
Swelling, > 50 mm, Dose 2(N-108,0)	0	0		
Pain, Any, Across doses (N-218,114)	82	54		
Pain, Grade 3, Across doses(N-218,114)	1	1		
Redness, Any, Across doses(N-218,114)	39	24		
Redness, > 50 mm, Across doses(N-218,114)	0	0		
Swelling, Any, Across doses(N-218,114)	44	39		
Swelling, > 50 mm, Across doses(N-218,114)	0	0		

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, Fever, Headache, Myalgia, Shivering and Sweating. Any= occurrence of the symptom regardless of intensity grade. Grade 3 fever = Grade 3 symptoms greater than (>) 39.0 °C. Related = symptoms considered by the investigator to have a causal relationship to study vaccination.

End point type	Secondary

End point timeframe:

During the 4-day (Day 0–3) post-vaccination period following each dose and across doses

End point values	Influsplit SSW 2005/2006 6-9 years Group	Influsplit SSW 2005/2006 10-13 years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	114		
Units: Participants				
Arthralgia, Any, Dose 1 (N-110,114)	10	6		
Arthralgia, Grade 3, Dose 1(N-110,114)	0	1		
Arthralgia, Related, Dose 1(N-110,114)	9	6		
Fatigue, Any, Dose 1(N-110,114)	22	22		
Fatigue, Grade 3, Dose 1(N-110,114)	0	0		
Fatigue, Related, Dose 1(N-110,114)	18	10		
Fever (Axillary), ≥ 37.5ºC,Dose 1(N-110,114)	3	3		
Fever (Axillary), > 39.0ºC, Dose 1(N-110,114)	0	0		
Fever (Axillary), Related, Dose 1(N-110,114)	3	3		
Headache, Any, Dose 1(N-110,114)	26	19		
Headache, Grade 3, Dose 1(N-110,114)	0	1		
Headache, Related, Dose 1(N-110,114)	19	10		
Myalgia, Any, Dose 1(N-110,114)	22	13		
Myalgia, Grade 3, Dose 1(N-110,114)	0	0		
Myalgia, Related, Dose 1(N-110,114)	19	10		
Shivering, Any, Dose 1(N-110,114)	10	8		
Shivering, Grade 3, Dose 1(N-110,114)	0	1		
Shivering, Related, Dose 1(N-110,114)	10	6		
Sweating, Any, Dose 1(N-110,114)	2	4		
Sweating, Grade 3, Dose 1(N-110,114)	0	0		
Sweating, Related, Dose 1(N-110,114)	2	3		
Arthralgia, Any, Dose 2 (N-108, 0)	3	0		
Arthralgia, Grade 3, Dose 2 (N-108, 0)	1	0		
Arthralgia, Related, Dose 2 (N-108, 0)	2	0		
Fatigue, Any, Dose 2 (N-108, 0)	12	0		
Fatigue, Grade 3, Dose 2 (N-108, 0)	1	0		
Fatigue, Related, Dose 2 (N-108, 0)	6	0		

Fever (Axillary), ≥ 37.5ºC, Dose 2(N-108, 0)	5	0		
Fever (Axillary), > 39.0ºC, Dose 2(N-108, 0)	0	0		
Fever (Axillary), Related, Dose 2(N-108, 0)	4	0		
Headache, Any, Dose 2(N-108, 0)	22	0		
Headache, Grade 3, Dose 2(N-108, 0)	2	0		
Headache, Related, Dose 2(N-108, 0)	16	0		
Myalgia, Any, Dose 2(N-108, 0)	19	0		
Myalgia, Grade 3, Dose 2(N-108, 0)	2	0		
Myalgia, Related, Dose 2(N-108, 0)	14	0		
Shivering, Any, Dose 2(N-108, 0)	8	0		
Shivering, Grade 3, Dose 2(N-108, 0)	1	0		
Shivering, Related, Dose 2(N-108, 0)	5	0		
Sweating, Any, Dose 2(N-108, 0)	3	0		
Sweating, Grade 3, Dose 2(N-108, 0)	0	0		
Sweating, Related, Dose 2(N-108, 0)	2	0		
Arthralgia, Any, Across doses(N-110,114)	13	6		
Arthralgia, Grade 3, Across doses(N-110,114)	1	1		
Arthralgia, Related, Across doses(N-110,114)	11	6		
Fatigue, Any, Across doses(N-110,114)	30	22		
Fatigue, Grade 3, Across doses(N-110,114)	1	0		
Fatigue, Related, Across doses(N-110,114)	22	10		
Fever (Axillary),≥ 37.5ºC,Across doses(N-110,114)	7	3		
Fever (Axillary),>39.0ºC,Across doses(N-110,114)	0	0		
Fever (Axillary), Related, Across doses(N-110,114)	6	3		
Headache, Any, Across doses(N-110,114)	38	19		
Headache, Grade 3, Across doses(N-110,114)	2	1		
Headache, Related, Across doses(N-110,114)	29	10		
Myalgia, Any, Across doses(N-110,114)	28	13		
Myalgia, Grade 3, Across doses(N-110,114)	2	0		
Myalgia, Related, Across doses(N-110,114)	23	10		
Shivering, Any, Across doses(N-110,114)	17	8		
Shivering, Grade 3, Across doses(N-110,114)	1	1		
Shivering, Related, Across doses(N-110,114)	14	6		
Sweating, Any, Across doses(N-110,114)	5	4		
Sweating, Grade 3, Across doses(N-110,114)	0	0		
Sweating, Related, Across doses(N-110,114)	4	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events.

End point title	Number of subjects with unsolicited adverse events.

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.

End point type	Secondary

End point timeframe:

During 31 days after the study vaccine dose (Day 0-30)

End point values	Influsplit SSW 2005/2006 6-9 years Group	Influsplit SSW 2005/2006 10-13 years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	114		
Units: Participants				
Subjects with any AE(s)(N-110,114)	52	30		
Subjects with Grade 3 AE(s)(N-110,114)	3	1		
Subjects with related AE(s)(N-110,114)	1	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

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

End point timeframe:

During the entire study period, from Day 0 to 58 + 5 days (30 + 5 days after the 2nd vaccine dose) for the 6-9 years Group and from Day 0 to 30 + 5 days (30 + 5 days after the vaccination) for the 10-13 years Group

End point values	Influsplit SSW 2005/2006 6-9 years Group	Influsplit SSW 2005/2006 10-13 years Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	114		
Units: Participants				
Any SAEs(N-110,114)	3	0		
Grade 3(N-110,114)	0	0		
Related SAEs(N-110,114)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs:During 4-day post-vaccination period after each dose & across doses. Unsolicited AEs:During 31 days after study vaccine dose.SAEs:During entire study period:Day 0-58+5 days for the 6-9 years Group & Day 0-30+5 days for the 10-13 years Group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Influsplit SSW 2005/2006 10-13 years Group

Reporting group description:

Subjects aged 10 to 13 years who received 1 dose of Influsplit SSW 2005/2006 vaccine at Day 0.

Reporting group title	Influsplit SSW 2005/2006 6-9 years Group

Reporting group description:

Subjects aged 6 to 9 years who received 2 doses of Influsplit SSW 2005/2006 vaccine at an interval of 4 weeks (Day 0 and Day 28 ± 2).

Serious adverse events	Influsplit SSW 2005/2006 10-13 years Group	Influsplit SSW 2005/2006 6-9 years Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 114 (0.00%)	3 / 110 (2.73%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Hereditary fructose intolerance			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			

subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Tonsillitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Influsplit SSW 2005/2006 10-13 years Group	Influsplit SSW 2005/2006 6-9 years Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 114 (78.95%)	100 / 110 (90.91%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Radius fracture			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Skin injury			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Nervous system disorders			

Headache			
subjects affected / exposed	19 / 114 (16.67%)	38 / 110 (34.55%)	
occurrences (all)	20	50	
General disorders and administration site conditions			
Axillary pain			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	8 / 114 (7.02%)	17 / 110 (15.45%)	
occurrences (all)	8	18	
Fatigue			
subjects affected / exposed	22 / 114 (19.30%)	30 / 110 (27.27%)	
occurrences (all)	22	34	
Injection site pruritus			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	54 / 114 (47.37%)	82 / 110 (74.55%)	
occurrences (all)	54	130	
Pyrexia			
subjects affected / exposed	4 / 114 (3.51%)	11 / 110 (10.00%)	
occurrences (all)	4	12	
Swelling			
subjects affected / exposed	39 / 114 (34.21%)	44 / 110 (40.00%)	
occurrences (all)	39	63	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Otosalpingitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	

Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Eye pruritus			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Ocular hyperaemia			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 114 (2.63%)	4 / 110 (3.64%)	
occurrences (all)	3	4	
Aphthous stomatitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 114 (0.88%)	4 / 110 (3.64%)	
occurrences (all)	1	6	
Dysphagia			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Enteritis			
subjects affected / exposed	0 / 114 (0.00%)	4 / 110 (3.64%)	
occurrences (all)	0	5	
Flatulence			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 114 (0.00%)	3 / 110 (2.73%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	2 / 114 (1.75%)	5 / 110 (4.55%)	
occurrences (all)	2	5	
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	5 / 114 (4.39%)	5 / 110 (4.55%)	
occurrences (all)	6	6	
Dyspnoea			
subjects affected / exposed	0 / 114 (0.00%)	3 / 110 (2.73%)	
occurrences (all)	0	3	
Pharyngeal erythema			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Pharyngolaryngeal pain			
subjects affected / exposed	2 / 114 (1.75%)	3 / 110 (2.73%)	
occurrences (all)	2	3	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	24 / 114 (21.05%)	39 / 110 (35.45%)	
occurrences (all)	24	59	
Hyperhidrosis			
subjects affected / exposed	4 / 114 (3.51%)	5 / 110 (4.55%)	
occurrences (all)	4	5	
Petechiae			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Rash			

subjects affected / exposed	2 / 114 (1.75%)	0 / 110 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 114 (5.26%)	13 / 110 (11.82%)	
occurrences (all)	7	13	
Back pain			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	13 / 114 (11.40%)	28 / 110 (25.45%)	
occurrences (all)	13	41	
Torticollis			
subjects affected / exposed	0 / 114 (0.00%)	2 / 110 (1.82%)	
occurrences (all)	0	2	
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 114 (0.88%)	2 / 110 (1.82%)	
occurrences (all)	1	2	
Ear infection			
subjects affected / exposed	0 / 114 (0.00%)	2 / 110 (1.82%)	
occurrences (all)	0	2	
Fungal infection			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	2 / 114 (1.75%)	1 / 110 (0.91%)	
occurrences (all)	2	2	
Lice infestation			

subjects affected / exposed	1 / 114 (0.88%)	2 / 110 (1.82%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	1 / 114 (0.88%)	2 / 110 (1.82%)	
occurrences (all)	1	2	
Otitis media			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	1 / 114 (0.88%)	7 / 110 (6.36%)	
occurrences (all)	1	8	
Sinusitis			
subjects affected / exposed	1 / 114 (0.88%)	0 / 110 (0.00%)	
occurrences (all)	1	0	
Streptococcal infection			
subjects affected / exposed	0 / 114 (0.00%)	3 / 110 (2.73%)	
occurrences (all)	0	3	
Tonsillitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	5 / 114 (4.39%)	13 / 110 (11.82%)	
occurrences (all)	5	14	
Viral infection			
subjects affected / exposed	0 / 114 (0.00%)	3 / 110 (2.73%)	
occurrences (all)	0	3	
Vulvitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 110 (0.91%)	
occurrences (all)	0	1	

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