Clinical trial results:
A Phase III, Randomized, Observer-blind, Multi-center, Noninferiority Comparison of the Immune Response of CSL Limited's Influenza Virus Vaccine Compared to a US Licensed Trivalent Inactivated Split-Virion Influenza Vaccine in a Pediatric Population Aged Greater Than or Equal to 6 Months to Less Than 18 Years.

Summary

EudraCT number	2014-003768-19
Trial protocol	Outside EU/EEA
Global end of trial date	03 May 2010

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	CSLCT-USF-07-36

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00959049
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Limited
Sponsor organisation address	45 Poplar Road, Parkville, Australia, VIC 3052
Public contact	Clinical Program Director, bioCSL, bioCSL PTY LTD, biocsl.clinicaltrials@biocsl.com.au
Scientific contact	Clinical Program Director, bioCSL, bioCSL PTY LTD, biocsl.clinicaltrials@biocsl.com.au

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 May 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2009
Global end of trial reached?	Yes
Global end of trial date	03 May 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that vaccination with CSL Limited’s Influenza Virus Vaccine (CSL’s IVV) elicits an immune response that is not inferior to that of a US licensed inactivated split-virion influenza vaccine (Fluzone®) in a pediatric population aged 6 months to less than 18 years.

Protection of trial subjects:

This study was conducted in accordance with standards of Good Clinical Practice, as defined by the International Conference on Harmonisation, the principles outlined in the Declaration of Helsinki and all applicable federal and local regulations.

Background therapy:

None

Evidence for comparator: -

Actual start date of recruitment	14 September 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 1474
Worldwide total number of subjects	1474
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	230
Children (2-11 years)	945
Adolescents (12-17 years)	299
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This prospective, randomized, observer-blind, multi-center, non-inferiority study was conducted in 1474 healthy children aged 6 months to less than 18 years at 23 sites in the US, during the Northern Hemisphere's 2009 autumn.

Pre-assignment

Screening details:

Healthy children were eligible for enrollment if they were aged 6 months to less than 18 years and were born at or after 36 weeks gestation (this criterion applied only to participants aged younger than 9 years) or returned a negative pregnancy test (this criterion applied only to female participants aged 9 years or older).

Period 1

Period 1 title	On-study period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The following study personnel were unblinded to treatment allocation:
• Investigational site staff involved in preparation and administration of the study vaccine;
• CRO personnel responsible for study vaccine preparation and management; and
• CRO personnel involved in the generation of the randomization code.

Arms

Are arms mutually exclusive?	Yes
Arm title	Afluria Cohort A

Arm description:

Age 6 months to < 3 years

Arm type	Experimental
Investigational medicinal product name	CSL's Influenza Virus Vaccine (Afluria)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.25 mL (one or two doses) by intramuscular injection as directed by immunization guidelines

Arm title	Afluria Cohort B

Arm description:

Age 3 to < 9 years

Arm type	Experimental
Investigational medicinal product name	CSL's Influenza Virus Vaccine (Afluria)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL (one or two doses) by intramuscular injection as directed by immunization guidelines

Arm title	Afluria Cohort C

Arm description:	
Age 9 to < 18 years	
Arm type	Experimental
Investigational medicinal product name	CSL's Influenza Virus Vaccine (Afluria)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
one 0.5 mL dose by intramuscular injection	
Arm title	Fluzone Cohort A
Arm description:	
Age 6 months to < 3 years	
Arm type	Active comparator
Investigational medicinal product name	Comparator US-Licensed Trivalent Influenza Vaccine (Fluzone)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
0.25 mL (one or two doses) by intramuscular injection as directed by immunization guidelines	
Arm title	Fluzone Cohort B
Arm description:	
Age 3 to < 9 years	
Arm type	Active comparator
Investigational medicinal product name	Comparator US-Licensed Trivalent Influenza Vaccine (Fluzone)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL (one or two doses) by intramuscular injection as directed by immunization guidelines	
Arm title	Fluzone Cohort C
Arm description:	
Age 9 to < 18 years	
Arm type	Active comparator
Investigational medicinal product name	Comparator US-Licensed Trivalent Influenza Vaccine (Fluzone)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
One 0.5 mL dose by intramuscular injection	

Number of subjects in period 1	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C
Started	231	254	254
Completed	213	247	253
Not completed	18	7	1
Adverse event, non-fatal	1	-	-
Lost to follow-up	17	5	1
Contraindicated medication	-	-	-
Withdrawal by subject	-	2	-

Number of subjects in period 1	Fluzone Cohort A	Fluzone Cohort B	Fluzone Cohort C
Started	228	257	250
Completed	217	248	249
Not completed	11	9	1
Adverse event, non-fatal	-	-	-
Lost to follow-up	10	9	1
Contraindicated medication	1	-	-
Withdrawal by subject	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Afluria Cohort A
Reporting group description:	
Age 6 months to < 3 years	
Reporting group title	Afluria Cohort B
Reporting group description:	
Age 3 to < 9 years	
Reporting group title	Afluria Cohort C
Reporting group description:	
Age 9 to < 18 years	
Reporting group title	Fluzone Cohort A
Reporting group description:	
Age 6 months to < 3 years	
Reporting group title	Fluzone Cohort B
Reporting group description:	
Age 3 to < 9 years	
Reporting group title	Fluzone Cohort C
Reporting group description:	
Age 9 to < 18 years	

Reporting group values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C
Number of subjects	231	254	254
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)	118	0	0
Children (2-11 years)	113	254	96
Adolescents (12-17 years)	0	0	158
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	1.94	5.93	12.98
standard deviation	± 0.667	± 1.725	± 2.388
Gender categorical Units: Subjects			
Female	119	140	121
Male	112	114	133

Reporting group values	Fluzone Cohort A	Fluzone Cohort B	Fluzone Cohort C
Number of subjects	228	257	250

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)	112	0	0
Children (2-11 years)	116	257	109
Adolescents (12-17 years)	0	0	141
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	1.96	5.82	12.86
standard deviation	± 0.673	± 1.748	± 2.474
Gender categorical Units: Subjects			
Female	101	127	120
Male	127	130	130

Reporting group values	Total		
Number of subjects	1474		
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)	230		
Children (2-11 years)	945		
Adolescents (12-17 years)	299		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	728		
Male	746		

End points

End points reporting groups	
Reporting group title	Afluria Cohort A
Reporting group description: Age 6 months to < 3 years	
Reporting group title	Afluria Cohort B
Reporting group description: Age 3 to < 9 years	
Reporting group title	Afluria Cohort C
Reporting group description: Age 9 to < 18 years	
Reporting group title	Fluzone Cohort A
Reporting group description: Age 6 months to < 3 years	
Reporting group title	Fluzone Cohort B
Reporting group description: Age 3 to < 9 years	
Reporting group title	Fluzone Cohort C
Reporting group description: Age 9 to < 18 years	

Primary: Geometric Mean Titer 30 Days After the Last Study Vaccination	
End point title	Geometric Mean Titer 30 Days After the Last Study Vaccination
End point description:	
End point type	Primary
End point timeframe: Geometric Mean Titer 30 Days After the Last Study Vaccination	

End point values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C	Fluzone Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	229	230	201
Units: Titers				
geometric mean (confidence interval 95%)				
H1N1 (A/Brisbane/59/2007)	235.44 (199.6 to 277.61)	345.5 (295.54 to 403.29)	652.99 (566.91 to 752.14)	227.19 (188.39 to 273.98)
H3N2 (A/Uruguay/716/2007)	309.19 (253.49 to 377.13)	909.22 (772.67 to 1069.9)	948.86 (824.88 to 1091.46)	340.49 (283.98 to 408.25)
B (B/Brisbane/60/2008)	73.46 (59.32 to 90.97)	122.71 (102.55 to 146.83)	107.92 (71.77 to 126.91)	57.92 (46.92 to 71.49)

End point values	Fluzone Cohort B	Fluzone Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	233		
Units: Titers				
geometric mean (confidence interval 95%)				
H1N1 (A/Brisbane/59/2007)	351.88 (303.29 to 408.25)	652.17 (569.59 to 746.73)		
H3N2 (A/Uruguay/716/2007)	870.34 (751.62 to 1007.8)	1069.7 (934.77 to 1224.11)		
B (B/Brisbane/60/2008)	104.91 (88.67 to 123.42)	126.99 (107.53 to 149.97)		

Statistical analyses

Statistical analysis title	Non-inferiority - H1N1 Strain

Statistical analysis description:

The non-inferiority of CSL's IVV compared with Fluzone was assessed by the co-primary endpoint of geometric mean titer (GMT) for each strain contained within the vaccines as follows:
• The GMT ratio for the H1N1 strain;
• The GMT ratio for the H3N2 strain;
• The GMT ratio for the B strain

Comparison groups	Afluria Cohort A v Fluzone Cohort A v Afluria Cohort B v Afluria Cohort C v Fluzone Cohort B v Fluzone Cohort C
Number of subjects included in analysis	1324
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	ratio of GMTs (H1N1 strain)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.04

Notes:

[1] - CSL's IVV was considered to be non-inferior to Fluzone if, for each strain:
• The upper bound of the two-sided 95% confidence interval (CI) on the ratio of the GMTs did not exceed 1.5-fold.
o The GMT ratio was calculated by using the geometric mean fold increase (GMFI):
GMFI Fluzone® / GMFI CSL's IVV where GMFI = GMT post-vaccination / GMT pre-vaccination

Statistical analysis title	Non-inferiority - H3N2 Strain

Statistical analysis description:

The non-inferiority of CSL's IVV compared with Fluzone was assessed by the co-primary endpoint of geometric mean titer (GMT) for each strain contained within the vaccines as follows:
• The GMT ratio for the H1N1 strain;
• The GMT ratio for the H3N2 strain;
• The GMT ratio for the B strain

Comparison groups	Afluria Cohort A v Fluzone Cohort A v Afluria Cohort B v Afluria Cohort C v Fluzone Cohort B v Fluzone Cohort C
Number of subjects included in analysis	1324
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	ratio of GMTs
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.23

Notes:

[2] - CSL's IVV was considered to be non-inferior to Fluzone if, for each strain:
• The upper bound of the two-sided 95% confidence interval (CI) on the ratio of the GMTs did not exceed 1.5-fold.
o The GMT ratio was calculated by using the geometric mean fold increase (GMFI):
GMFI Fluzone® / GMFI CSL's IVV where GMFI = GMT post-vaccination / GMT pre-vaccination

Statistical analysis title	Non-inferiority - B Strain

Statistical analysis description:

The non-inferiority of CSL's IVV compared with Fluzone was assessed by the co-primary endpoint of geometric mean titer (GMT) for each strain contained within the vaccines as follows:
• The GMT ratio for the H1N1 strain;
• The GMT ratio for the H3N2 strain;
• The GMT ratio for the B strain

Comparison groups	Afluria Cohort A v Fluzone Cohort A v Afluria Cohort B v Afluria Cohort C v Fluzone Cohort B v Fluzone Cohort C
Number of subjects included in analysis	1324
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	ratio of GMTs
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.07

Notes:

[3] - CSL's IVV was considered to be non-inferior to Fluzone if, for each strain:
• The upper bound of the two-sided 95% confidence interval (CI) on the ratio of the GMTs did not exceed 1.5-fold.
o The GMT ratio was calculated by using the geometric mean fold increase (GMFI):
GMFI Fluzone® / GMFI CSL's IVV where GMFI = GMT post-vaccination / GMT pre-vaccination

Primary: Percentage of Participants With Seroconversion 30 Days After the Last Study Vaccination

End point title	Percentage of Participants With Seroconversion 30 Days After the Last Study Vaccination

End point description:

Seroconversion rate was defined as the proportion of participants with either a titer of less than 1:10 before vaccination achieving a HI antibody titer of 1:40 or more after vaccination, or a HI titer of 1:10 or more before vaccination achieving a four-fold or greater increase in HI titer after vaccination.

End point type	Primary

End point timeframe:

30 days after the last study vaccination

End point values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C	Fluzone Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	195	229	230	201
Units: percentage of participants				
number (confidence interval 95%)				
H1N1 (A/Brisbane/59/2007)	84 (78 to 89)	66 (59 to 72)	64 (57 to 70)	74 (67 to 80)
H3N2 (A/Uruguay/716/2007)	83 (77 to 88)	71 (65 to 77)	72 (66 to 78)	85 (79 to 90)
B (B/Brisbane/60/2008)	67 (60 to 73)	73 (67 to 79)	67 (31 to 73)	61 (54 to 68)

End point values	Fluzone Cohort B	Fluzone Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	233		
Units: percentage of participants				
number (confidence interval 95%)				
H1N1 (A/Brisbane/59/2007)	64 (58 to 70)	61 (55 to 68)		
H3N2 (A/Uruguay/716/2007)	74 (68 to 80)	73 (66 to 78)		
B (B/Brisbane/60/2008)	76 (70 to 82)	73 (67 to 79)		

Statistical analyses

Statistical analysis title	Non-inferiority - H1N1 Strain

Statistical analysis description:

Non-inferiority of CSL's IVV compared with Fluzone was assessed by the co-primary endpoint of seroconversion rate for each strain contained within the vaccines as follows:
• The difference between the seroconversion rates for the H1N1 strain;
• The difference between the seroconversion rates for the H3N2 strain;
• The difference between the seroconversion rates for the B strain

Comparison groups	Fluzone Cohort A v Afluria Cohort B v Afluria Cohort A v Afluria Cohort C v Fluzone Cohort B v Fluzone Cohort C
Number of subjects included in analysis	1324
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in seroconversion rates
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	-0.9

Notes:

[4] - CSL's IVV was considered to be non-inferior to Fluzone if, for each strain:
The upper bound of the two-sided 95% CI on the difference between the seroconversion rates did not exceed 10 percentage points.
The difference in seroconversion rates was calculated by: Seroconversion Fluzone – Seroconversion CSL'

s IVV.

Statistical analysis title	Non-inferiority - H3N2 Strain

Statistical analysis description:

Non-inferiority of CSL's IVV compared with Fluzone was assessed by the co-primary endpoint of seroconversion rate for each strain contained within the vaccines as follows:
• The difference between the seroconversion rates for the H1N1 strain;
• The difference between the seroconversion rates for the H3N2 strain;
• The difference between the seroconversion rates for the B strain

Comparison groups	Afluria Cohort A v Fluzone Cohort A v Afluria Cohort B v Afluria Cohort C v Fluzone Cohort B v Fluzone Cohort C
Number of subjects included in analysis	1324
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in seroconversion rates
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	6.5

Notes:

[5] - CSL's IVV was considered to be non-inferior to Fluzone if, for each strain:
The upper bound of the two-sided 95% CI on the difference between the seroconversion rates did not exceed 10 percentage points.
The difference in seroconversion rates was calculated by: Seroconversion Fluzone – Seroconversion CSL' s IVV.

Statistical analysis title	Non-inferiority - B Strain

Statistical analysis description:

Non-inferiority of CSL's IVV compared with Fluzone was assessed by the co-primary endpoint of seroconversion rate for each strain contained within the vaccines as follows:
• The difference between the seroconversion rates for the H1N1 strain;
• The difference between the seroconversion rates for the H3N2 strain;
• The difference between the seroconversion rates for the B strain

Comparison groups	Afluria Cohort A v Fluzone Cohort A v Afluria Cohort B v Afluria Cohort C v Fluzone Cohort B v Fluzone Cohort C
Number of subjects included in analysis	1324
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in seroconversion rates
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	6.3

Notes:

[6] - CSL's IVV was considered to be non-inferior to Fluzone if, for each strain:
The upper bound of the two-sided 95% CI on the difference between the seroconversion rates did not exceed 10 percentage points.
The difference in seroconversion rates was calculated by: Seroconversion Fluzone – Seroconversion CSL' s IVV.

Secondary: Frequency and Intensity of Local and Systemic Solicited Symptoms after Any Vaccination

End point title	Frequency and Intensity of Local and Systemic Solicited Symptoms after Any Vaccination

End point description:

Note that the systemic solicited symptoms of loss of appetite and irritability were collected for Afluria cohort A and Fluzone Cohort A only, and malaise, headache and myalgia were not collected for these two cohorts. Afluria Cohort C and Fluzone Cohort C received one dose only. Abbreviations: pd1= post-dose 1, pd2=post-dose 2.

End point type	Secondary

End point timeframe:

7 days after each vaccination

End point values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C	Fluzone Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	252	254[7]	228
Units: Number of participants				
Any local solicited symptom post-dose 1	116	164	174	100
Any pain post-dose 1	98	149	167	78
Grade 3 pain post-dose 1	1	1	1	0
Any redness (> 0 mm) post-dose 1	53	59	43	53
Grade 3 redness (> 30 mm) post-dose 1	0	7	1	1
Any swelling (> 0 mm) post-dose 1	30	36	39	26
Grade 3 swelling (> 30 mm) post-dose 1	1	6	4	0
Any local solicited symptom post-dose 2	30	24	0	32
Any pain post-dose 2	28	23	0	22
Grade 3 pain post-dose 2	0	0	0	0
Any redness (> 0 mm) post-dose 2	15	5	0	22
Grade 3 redness (> 30 mm) post-dose 2	1	0	0	0
Any swelling (> 0 mm) post-dose 2	9	4	0	7
Grade 3 swelling (> 30 mm) post-dose 2	0	0	0	0
Any systemic solicited symptom post-dose 1	171	140	144	121
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) post-dos	85	55	16	31
Grade 3 fever (> 103.1°F ax or > 104.0°F oral) pos	6	3	2	0
Any nausea/vomiting post-dose 1	27	33	23	17
Grade 3 nausea/vomiting (prevented activities) pos	6	2	3	1
Any diarrhea post-dose 1	61	17	20	54
Grade 3 diarrhea (prevented activities) postdose1	4	0	1	3
Any loss of appetite post-dose 1	73	0	0	45
Grade 3 loss of appetite (prevented activities) p1	3	0	0	1
Any irritability post-dose 1	134	0	0	85
Grade 3 irritability (prevented activities) pd1	10	0	0	5
Any malaise post-dose 1	0	72	55	0

Grade 3 malaise (prevented activities) pd1	0	9	10	0
Any headache post-dose 1	0	54	69	0
Grade 3 headache (prevented activities) pd1	0	5	7	0
Any myalgia post-dose 1	0	82	101	0
Grade 3 myalgia (prevented activities) pd1	0	1	5	0
Any systemic solicited symptom post-dose 2	48	17	0	44
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) pd2	14	4	0	15
Grade 3 fever (> 103.1°F ax or > 104.0°F oral) pd2	1	1	0	0
Any nausea/vomiting post-dose 2	4	2	0	8
Grade 3 nausea/vomiting (prevented activities) pd2	2	1	0	0
Any diarrhea post-dose 2	17	6	0	16
Grade 3 diarrhea post-dose 2	1	0	0	0
Any loss of appetite post-dose 2	15	0	0	14
Grade 3 loss of appetite post-dose 2	1	0	0	0
Any irritability post-dose 2	38	0	0	31
Grade 3 irritability post-dose 2	1	0	0	0
Any malaise post-dose 2	0	6	0	0
Grade 3 malaise post-dose 2	0	0	0	0
Any headache post-dose 2	0	6	0	0
Grade 3 headache post-dose 2	0	0	0	0
Any myalgia post-dose 2	0	7	0	0
Grade 3 myalgia post-dose 2	0	0	0	0

Notes:

[7] - Age 9 to < 18 years - one dose only

End point values	Fluzone Cohort B	Fluzone Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	250		
Units: Number of participants				
Any local solicited symptom post-dose 1	152	169		
Any pain post-dose 1	131	151		
Grade 3 pain post-dose 1	4	4		
Any redness (> 0 mm) post-dose 1	60	43		
Grade 3 redness (> 30 mm) post-dose 1	4	3		
Any swelling (> 0 mm) post-dose 1	43	41		
Grade 3 swelling (> 30 mm) post-dose 1	2	7		
Any local solicited symptom post-dose 2	26	0		
Any pain post-dose 2	23	0		
Grade 3 pain post-dose 2	0	0		
Any redness (> 0 mm) post-dose 2	13	0		
Grade 3 redness (> 30 mm) post-dose 2	0	0		
Any swelling (> 0 mm) post-dose 2	11	0		
Grade 3 swelling (> 30 mm) post-dose 2	0	0		

Any systemic solicited symptom post-dose 1	113	126		
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) post-dos	24	10		
Grade 3 fever (> 103.1°F ax or > 104.0°F oral) pos	1	0		
Any nausea/vomiting post-dose 1	20	24		
Grade 3 nausea/vomiting (prevented activities) pos	1	3		
Any diarrhea post-dose 1	24	25		
Grade 3 diarrhea (prevented activities) postdose1	0	0		
Any loss of appetite post-dose 1	0	0		
Grade 3 loss of appetite (prevented activities) p1	0	0		
Any irritability post-dose 1	0	0		
Grade 3 irritability (prevented activities) pd1	0	0		
Any malaise post-dose 1	34	51		
Grade 3 malaise (prevented activities) pd1	1	3		
Any headache post-dose 1	41	66		
Grade 3 headache (prevented activities) pd1	0	3		
Any myalgia post-dose 1	63	93		
Grade 3 myalgia (prevented activities) pd1	1	4		
Any systemic solicited symptom post-dose 2	18	0		
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) pd2	5	0		
Grade 3 fever (> 103.1°F ax or > 104.0°F oral) pd2	0	0		
Any nausea/vomiting post-dose 2	4	0		
Grade 3 nausea/vomiting (prevented activities) pd2	0	0		
Any diarrhea post-dose 2	5	0		
Grade 3 diarrhea post-dose 2	0	0		
Any loss of appetite post-dose 2	0	0		
Grade 3 loss of appetite post-dose 2	0	0		
Any irritability post-dose 2	0	0		
Grade 3 irritability post-dose 2	0	0		
Any malaise post-dose 2	6	0		
Grade 3 malaise post-dose 2	0	0		
Any headache post-dose 2	8	0		
Grade 3 headache post-dose 2	0	0		
Any myalgia post-dose 2	12	0		
Grade 3 myalgia post-dose 2	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency and Intensity of Unsolicited Adverse Events (UAEs)

End point title	Frequency and Intensity of Unsolicited Adverse Events (UAEs)

End point description:

End point type	Secondary

End point timeframe:

30 days after each vaccination

End point values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C	Fluzone Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	252	254	228
Units: Number of participants				
Any UAE	123	100	88	112
Grade 3 UAE	28	25	17	24
Any related UAE	37	24	20	16

End point values	Fluzone Cohort B	Fluzone Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	250		
Units: Number of participants				
Any UAE	84	70		
Grade 3 UAE	22	16		
Any related UAE	18	14		

Statistical analyses

No statistical analyses for this end point

Secondary: New Onset of Chronic Illnesses (NOCIs)

End point title	New Onset of Chronic Illnesses (NOCIs)

End point description:

New onset of chronic illness after any vaccine dose: A new onset of chronic illness was defined as the diagnosis of a new medical condition which was chronic in nature, including those potentially controllable by medication (eg, diabetes, asthma).

End point type	Secondary

End point timeframe:

6 months after last study vaccination

End point values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C	Fluzone Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	252	254	228
Units: Number of participants				
Total number of participants with NOCI	2	0	2	2
Number of participants with related NOCI	0	0	0	0
Asthma	1	0	2	1
Von Willebrand's Disease	1	0	0	0
Eczema	0	0	0	1
Attention deficit disorder	0	0	0	0

End point values	Fluzone Cohort B	Fluzone Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	250		
Units: Number of participants				
Total number of participants with NOCI	1	0		
Number of participants with related NOCI	0	0		
Asthma	0	0		
Von Willebrand's Disease	0	0		
Eczema	0	0		
Attention deficit disorder	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Serious Adverse Events (SAEs)

End point title	Serious Adverse Events (SAEs)

End point description:

End point type	Secondary

End point timeframe:

6 months after last study vaccination

End point values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C	Fluzone Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	252	254	228
Units: Number of participants				
SAEs	4	2	2	4
Related SAEs	0	0	0	0

End point values	Fluzone Cohort B	Fluzone Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	250		
Units: Number of participants				
SAEs	0	0		
Related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Local and Systemic Solicited Symptoms

End point title	Duration of Local and Systemic Solicited Symptoms

End point description:

Note that the systemic solicited symptoms of loss of appetite and irritability were collected for Afluria cohort A and Fluzone Cohort A only, and malaise, headache and myalgia were not collected for these two cohorts. Afluria Cohort C and Fluzone Cohort C received one dose only.

End point type	Secondary

End point timeframe:

7 days after each vaccination

End point values	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C	Fluzone Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	252	254	228
Units: Days				
arithmetic mean (standard deviation)				
Any pain post-dose 1	1.57 (± 0.952)	1.89 (± 1.138)	1.96 (± 1.087)	1.43 (± 0.728)
Any redness (> 0 mm) post-dose 1	2.09 (± 1.405)	2.32 (± 1.621)	2.02 (± 1.669)	2.22 (± 1.939)
Any swelling (> 0 mm) post-dose 1	3.13 (± 2.93)	2.39 (± 2.021)	1.75 (± 1.171)	2 (± 1.569)
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) pd1	1.38 (± 0.869)	1.45 (± 1.032)	1.82 (± 1.59)	1.49 (± 0.989)
Any nausea/vomiting post-dose 1	1.42 (± 1.119)	1.27 (± 0.719)	1.36 (± 0.569)	1.29 (± 1.042)
Any diarrhea post-dose 1	2.23 (± 2.157)	2.89 (± 4.988)	1.18 (± 0.395)	2.16 (± 2.189)
Any malaise post-dose 1	0 (± 0)	1.86 (± 1.324)	2.09 (± 1.487)	0 (± 0)
Any headache post-dose 1	0 (± 0)	1.5 (± 0.77)	1.77 (± 1.443)	0 (± 0)
Any myalgia post-dose 1	0 (± 0)	1.72 (± 1.007)	1.76 (± 1.1)	0 (± 0)
Any loss of appetite post-dose 1	2.61 (± 3.695)	0 (± 0)	0 (± 0)	2.85 (± 4.458)
Any irritability post-dose 1	2.26 (± 2.858)	0 (± 0)	0 (± 0)	2.64 (± 3.825)
Any pain post-dose 2	1.54 (± 0.793)	1.96 (± 1.637)	0 (± 0)	1.45 (± 0.739)
Any redness (> 0 mm) post-dose 2	1.8 (± 1.014)	2.4 (± 2.191)	0 (± 0)	1.73 (± 0.935)
Any swelling (> 0 mm) post-dose 2	1.67 (± 0.707)	3 (± 2.16)	0 (± 0)	1.57 (± 0.787)
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) pd2	1.8 (± 1.146)	1.5 (± 0.577)	0 (± 0)	1.81 (± 1.559)

Any nausea/vomiting post-dose 2	2.5 (± 1.291)	1 (± 0)	0 (± 0)	1.78 (± 1.093)
Any diarrhea post-dose 2	2.83 (± 2.431)	1.33 (± 0.816)	0 (± 0)	2.44 (± 2.332)
Any malaise post-dose 2	0 (± 0)	1.83 (± 1.602)	0 (± 0)	0 (± 0)
Any headache post-dose 2	0 (± 0)	1 (± 0)	0 (± 0)	0 (± 0)
Any myalgia post-dose 2	0 (± 0)	2 (± 1.528)	0 (± 0)	0 (± 0)
Any loss of appetite post-dose 2	2.47 (± 1.586)	0 (± 0)	0 (± 0)	2.33 (± 1.447)
Any irritability post-dose 2	2.31 (± 1.732)	0 (± 0)	0 (± 0)	2.17 (± 1.543)

End point values	Fluzone Cohort B	Fluzone Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	250		
Units: Days				
arithmetic mean (standard deviation)				
Any pain post-dose 1	1.89 (± 1.337)	1.99 (± 1.136)		
Any redness (> 0 mm) post-dose 1	2.1 (± 2.014)	2.38 (± 1.992)		
Any swelling (> 0 mm) post-dose 1	2.09 (± 1.273)	2.38 (± 1.724)		
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) pd1	1.4 (± 0.707)	3.1 (± 2.644)		
Any nausea/vomiting post-dose 1	1.43 (± 1.165)	2.88 (± 3.791)		
Any diarrhea post-dose 1	1.44 (± 1.044)	1.36 (± 0.911)		
Any malaise post-dose 1	1.74 (± 1.094)	2.82 (± 3.449)		
Any headache post-dose 1	1.66 (± 1.328)	2.05 (± 1.945)		
Any myalgia post-dose 1	1.63 (± 1.009)	2.11 (± 1.491)		
Any loss of appetite post-dose 1	0 (± 0)	0 (± 0)		
Any irritability post-dose 1	0 (± 0)	0 (± 0)		
Any pain post-dose 2	1.65 (± 0.775)	0 (± 0)		
Any redness (> 0 mm) post-dose 2	1.77 (± 1.235)	0 (± 0)		
Any swelling (> 0 mm) post-dose 2	1.69 (± 1.251)	0 (± 0)		
Any fever (≥ 99.5°F ax or ≥ 100.4°F oral) pd2	1 (± 0)	0 (± 0)		
Any nausea/vomiting post-dose 2	1.2 (± 0.447)	0 (± 0)		
Any diarrhea post-dose 2	2.2 (± 0.447)	0 (± 0)		
Any malaise post-dose 2	1.71 (± 0.756)	0 (± 0)		
Any headache post-dose 2	1.3 (± 0.483)	0 (± 0)		
Any myalgia post-dose 2	1.54 (± 0.66)	0 (± 0)		
Any loss of appetite post-dose 2	0 (± 0)	0 (± 0)		
Any irritability post-dose 2	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse event data were collected for 180 days after the last study vaccination.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.0
Reporting groups	
Reporting group title	Afluria Cohort A
Reporting group description: Age 6 months to < 3 years	
Reporting group title	Afluria Cohort B
Reporting group description: Age 3 to < 9 years	
Reporting group title	Afluria Cohort C
Reporting group description: Age 9 to < 18 years	
Reporting group title	Fluzone Cohort A
Reporting group description: Age 6 months to < 3 years	
Reporting group title	Fluzone Cohort B
Reporting group description: Age 3 to < 9 years	
Reporting group title	Fluzone Cohort C
Reporting group description: Age 9 to < 18 years	

Serious adverse events	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 229 (1.75%)	2 / 252 (0.79%)	2 / 254 (0.79%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 252 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colonic polyp			

subjects affected / exposed	0 / 229 (0.00%)	1 / 252 (0.40%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 229 (0.00%)	1 / 252 (0.40%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 229 (0.44%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 229 (0.44%)	1 / 252 (0.40%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 229 (0.44%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 252 (0.00%)	1 / 254 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 229 (0.00%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Furuncle			
subjects affected / exposed	0 / 229 (0.00%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 229 (0.44%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Fluzone Cohort A	Fluzone Cohort B	Fluzone Cohort C
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 228 (1.75%)	0 / 255 (0.00%)	0 / 250 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 228 (0.00%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colonic polyp			
subjects affected / exposed	0 / 228 (0.00%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 228 (0.00%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 228 (0.00%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	0 / 228 (0.00%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 228 (0.00%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	1 / 228 (0.44%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Furuncle			
subjects affected / exposed	1 / 228 (0.44%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 228 (0.00%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Afluria Cohort A	Afluria Cohort B	Afluria Cohort C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	210 / 229 (91.70%)	216 / 252 (85.71%)	214 / 254 (84.25%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 229 (2.62%)	6 / 252 (2.38%)	17 / 254 (6.69%)
occurrences (all)	7	6	22
General disorders and administration site conditions			
Pain at the injection site			
alternative assessment type: Systematic			
subjects affected / exposed	107 / 229 (46.72%)	157 / 252 (62.30%)	167 / 254 (65.75%)
occurrences (all)	126	174	170
Redness at the injection site			
alternative assessment type: Systematic			
subjects affected / exposed	60 / 229 (26.20%)	62 / 252 (24.60%)	43 / 254 (16.93%)
occurrences (all)	70	65	43
Swelling at the injection site			
alternative assessment type: Systematic			
subjects affected / exposed	34 / 229 (14.85%)	38 / 252 (15.08%)	39 / 254 (15.35%)
occurrences (all)	40	42	40
Fever			
subjects affected / exposed	91 / 229 (39.74%)	58 / 252 (23.02%)	16 / 254 (6.30%)
occurrences (all)	109	64	17
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	79 / 229 (34.50%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences (all)	100	0	0
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	142 / 229 (62.01%)	0 / 252 (0.00%)	0 / 254 (0.00%)
occurrences (all)	198	0	0
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 229 (0.00%)	74 / 252 (29.37%)	55 / 254 (21.65%)
occurrences (all)	0	82	65

Headache (solicited)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 229 (0.00%)	58 / 252 (23.02%)	69 / 254 (27.17%)
occurrences (all)	0	66	81
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 229 (0.00%)	87 / 252 (34.52%)	101 / 254 (39.76%)
occurrences (all)	0	92	106
Pyrexia			
subjects affected / exposed	32 / 229 (13.97%)	24 / 252 (9.52%)	12 / 254 (4.72%)
occurrences (all)	34	29	18
Gastrointestinal disorders			
Nausea and vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 229 (13.54%)	35 / 252 (13.89%)	23 / 254 (9.06%)
occurrences (all)	35	36	25
Diarrhea (solicited)			
alternative assessment type: Systematic			
subjects affected / exposed	69 / 229 (30.13%)	22 / 252 (8.73%)	20 / 254 (7.87%)
occurrences (all)	87	25	22
Diarrhea			
subjects affected / exposed	10 / 229 (4.37%)	3 / 252 (1.19%)	4 / 254 (1.57%)
occurrences (all)	11	3	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	39 / 229 (17.03%)	40 / 252 (15.87%)	19 / 254 (7.48%)
occurrences (all)	44	40	22
Rhinorrhoea			
subjects affected / exposed	25 / 229 (10.92%)	14 / 252 (5.56%)	5 / 254 (1.97%)
occurrences (all)	28	14	6
Nasal congestion			
subjects affected / exposed	14 / 229 (6.11%)	8 / 252 (3.17%)	16 / 254 (6.30%)
occurrences (all)	16	8	17
Oropharyngeal pain			

subjects affected / exposed	4 / 229 (1.75%)	7 / 252 (2.78%)	19 / 254 (7.48%)
occurrences (all)	4	7	23
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	9 / 229 (3.93%)	6 / 252 (2.38%)	4 / 254 (1.57%)
occurrences (all)	9	6	4

Non-serious adverse events	Fluzone Cohort A	Fluzone Cohort B	Fluzone Cohort C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	187 / 228 (82.02%)	202 / 255 (79.22%)	202 / 250 (80.80%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 228 (1.32%)	8 / 255 (3.14%)	12 / 250 (4.80%)
occurrences (all)	3	8	13
General disorders and administration site conditions			
Pain at the injection site			
alternative assessment type: Systematic			
subjects affected / exposed	89 / 228 (39.04%)	134 / 255 (52.55%)	151 / 250 (60.40%)
occurrences (all)	101	154	156
Redness at the injection site			
alternative assessment type: Systematic			
subjects affected / exposed	60 / 228 (26.32%)	67 / 255 (26.27%)	43 / 250 (17.20%)
occurrences (all)	76	73	45
Swelling at the injection site			
alternative assessment type: Systematic			
subjects affected / exposed	29 / 228 (12.72%)	50 / 255 (19.61%)	41 / 250 (16.40%)
occurrences (all)	34	57	42
Fever			
subjects affected / exposed	42 / 228 (18.42%)	29 / 255 (11.37%)	10 / 250 (4.00%)
occurrences (all)	53	32	10
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 228 (23.68%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences (all)	63	0	0
Irritability			
alternative assessment type: Systematic			

subjects affected / exposed	99 / 228 (43.42%)	0 / 255 (0.00%)	0 / 250 (0.00%)
occurrences (all)	132	0	0
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 228 (0.00%)	37 / 255 (14.51%)	51 / 250 (20.40%)
occurrences (all)	0	42	55
Headache (solicited)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 228 (0.00%)	45 / 255 (17.65%)	66 / 250 (26.40%)
occurrences (all)	0	54	76
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 228 (0.00%)	66 / 255 (25.88%)	93 / 250 (37.20%)
occurrences (all)	0	78	98
Pyrexia			
subjects affected / exposed	22 / 228 (9.65%)	17 / 255 (6.67%)	7 / 250 (2.80%)
occurrences (all)	23	18	9
Gastrointestinal disorders			
Nausea and vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 228 (10.09%)	24 / 255 (9.41%)	24 / 250 (9.60%)
occurrences (all)	33	26	24
Diarrhea (solicited)			
alternative assessment type: Systematic			
subjects affected / exposed	63 / 228 (27.63%)	27 / 255 (10.59%)	25 / 250 (10.00%)
occurrences (all)	80	30	28
Diarrhea			
subjects affected / exposed	13 / 228 (5.70%)	3 / 255 (1.18%)	1 / 250 (0.40%)
occurrences (all)	14	3	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	31 / 228 (13.60%)	33 / 255 (12.94%)	17 / 250 (6.80%)
occurrences (all)	39	36	19
Rhinorrhoea			

subjects affected / exposed	24 / 228 (10.53%)	10 / 255 (3.92%)	5 / 250 (2.00%)
occurrences (all)	29	10	5
Nasal congestion			
subjects affected / exposed	11 / 228 (4.82%)	4 / 255 (1.57%)	6 / 250 (2.40%)
occurrences (all)	12	4	7
Oropharyngeal pain			
subjects affected / exposed	2 / 228 (0.88%)	6 / 255 (2.35%)	13 / 250 (5.20%)
occurrences (all)	2	6	15
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	14 / 228 (6.14%)	5 / 255 (1.96%)	4 / 250 (1.60%)
occurrences (all)	16	5	4

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25454878