Clinical trial results:
Immunogenicity and Safety of Sanofi Pasteur's AVAXIM 80U Pediatric Vaccine Administered in Healthy Adolescents, Children and Toddlers in People's Republic of China Followed by a Booster Dose 6 Months after the Initial Dose Versus HAVRIX 720 Vaccine

Summary

EudraCT number	2015-005191-18
Trial protocol	Outside EU/EEA
Global end of trial date	08 March 2008

Results information

Result version number	v1 (current)
This version publication date	26 March 2016
First version publication date	26 March 2016

Trial information

Trial identification

Sponsor protocol code	HAF78

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00483470
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Responsible Medical Officer, Sanofi Pasteur SA, 33 4 37 37 73 84, Eric.desauziers@sanofipasteur.com
Scientific contact	Responsible Medical Officer, Sanofi Pasteur SA, 33 4 37 37 73 84, Eric.desauziers@sanofipasteur.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 June 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 March 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To demonstrate the non-inferiority in terms of seroprotection rate of AVAXIM 80U Pediatric vaccine versus HAVRIX 720 vaccine 1 month after booster vaccination.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	30 May 2007
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	China: 720
Worldwide total number of subjects	720
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)	78
Children (2-11 years)	376
Adolescents (12-17 years)	266
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study subjects were enrolled from 06 June 2007 to 15 August 2007 at 1 clinic center in China.

Pre-assignment

Screening details:

A total of 720 subjects who met all of the inclusion and none of the exclusion criteria were randomized and vaccinated in this study.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A; AVAXIM 80U Pediatric

Arm description:

Subjects received AVAXIM 80U Pediatric vaccine at baseline and a booster dose 6 months after the primary injection.

Arm type	Experimental
Investigational medicinal product name	Hepatitis A vaccine (AVAXIM 80U Pediatric)
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, intramuscular into the left deltoid muscle, 1 injection on Day 0 and as a booster dose 6 months after the primary injection.

Arm title	Group B; HAVRIX 720

Arm description:

Subjects received HAVRIX 720 vaccine at baseline and a booster dose 6 months after the primary injection.

Arm type	Active comparator
Investigational medicinal product name	Hepatitis A vaccine (HAVRIX 720)
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, intramuscular, 1 injection on Day 0 and as a booster dose 6 months after the primary injection.

Number of subjects in period 1	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720
Started	480	240
Completed	457	229
Not completed	23	11
Consent withdrawn by subject	13	8
Lost to follow-up	4	2
Protocol deviation	6	1

Baseline characteristics

Reporting groups	
Reporting group title	Group A; AVAXIM 80U Pediatric
Reporting group description:	
Subjects received AVAXIM 80U Pediatric vaccine at baseline and a booster dose 6 months after the primary injection.	
Reporting group title	Group B; HAVRIX 720
Reporting group description:	
Subjects received HAVRIX 720 vaccine at baseline and a booster dose 6 months after the primary injection.	

Reporting group values	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720	Total
Number of subjects	480	240	720
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)	54	24	78
Children (2-11 years)	247	129	376
Adolescents (12-17 years)	179	87	266
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	8.78	8.81	
standard deviation	± 4.5	± 4.43	-
Gender categorical Units: Subjects			
Female	246	118	364
Male	234	122	356

End points

End points reporting groups

Reporting group title	Group A; AVAXIM 80U Pediatric
Reporting group description:	
Subjects received AVAXIM 80U Pediatric vaccine at baseline and a booster dose 6 months after the primary injection.	
Reporting group title	Group B; HAVRIX 720
Reporting group description:	
Subjects received HAVRIX 720 vaccine at baseline and a booster dose 6 months after the primary injection.	

Primary: Percentage of Subjects With Seroprotection Against Inactivated Hepatitis A Antigen After Primary and Booster Vaccinations with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine

End point title	Percentage of Subjects With Seroprotection Against Inactivated Hepatitis A Antigen After Primary and Booster Vaccinations with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine
End point description:	
Anti-Hepatitis A antibody titers were measured by enzyme-linked immunosorbent assay (ELISA). Seroprotection was defined as Anti-Hepatitis A virus antibody titers ≥ 20 mIU/mL on Day 210, 1 month after booster vaccination with study vaccines. Seroprotection is reported based on age group: Toddlers (12 to 23 months), Children (2 to 11 years), and Adolescents (12 to 15 years).	
End point type	Primary
End point timeframe:	
Day 210 (1 month post booster vaccination)	

End point values	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	454	226		
Units: Percentage of subjects				
number (not applicable)				
All Subjects; Anti-Hepatitis A antibody titers	99.8	100		
Toddlers; Anti-Hepatitis A antibody titers	100	100		
Children; Anti-Hepatitis A antibody titers	100	100		
Adolescents; Anti-Hepatitis A antibody titers	99.4	100		

Statistical analyses

Statistical analysis title	Non-inferiority (Group A - Group B); All Subjects
Statistical analysis description:	
Non-inferiority analysis of AVAXIM 80U Pediatric on HAVRIX 720 in all subjects assessed 1 month after	

booster vaccination.

Comparison groups	Group A; AVAXIM 80U Pediatric v Group B; HAVRIX 720
Number of subjects included in analysis	680
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in AVAXIM 80U Ped.-HAVRIX 720
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	1.46

Notes:

[1] - The non-inferiority was demonstrated if the lower bound of the two-sided 95% confidence interval (CI) of the difference was greater than -10%. The 95% CI was calculated with the Wilson score method without continuity correction. AVAXIM 80U Pediatric was non-inferior to HAVRIX 720.

Statistical analysis title	Non-inferiority (Group A - Group B); Toddlers

Statistical analysis description:

Non-inferiority analysis of AVAXIM 80U Pediatric on HAVRIX 720 in toddlers (12 to 23 months) assessed 1 month after booster vaccination.

Comparison groups	Group A; AVAXIM 80U Pediatric v Group B; HAVRIX 720
Number of subjects included in analysis	680
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in AVAXIM 80U Ped.-HAVRIX 720
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.41
upper limit	15.46

Notes:

[2] - The non-inferiority was demonstrated if the lower bound of the two-sided 95% confidence interval (CI) of the difference was greater than -10%. The 95% CI was calculated with the Wilson score method without continuity correction. AVAXIM 80U Pediatric was non-inferior to HAVRIX 720.

Statistical analysis title	Non-inferiority (Group A - Group B); Children

Statistical analysis description:

Non-inferiority analysis of AVAXIM 80U Pediatric on HAVRIX 720 in children (2 to 11 years) assessed 1 month after booster vaccination.

Comparison groups	Group A; AVAXIM 80U Pediatric v Group B; HAVRIX 720
Number of subjects included in analysis	680
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in AVAXIM 80U Ped.-HAVRIX 720
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	2.98

Notes:

[3] - The non-inferiority was demonstrated if the lower bound of the two-sided 95% confidence interval (CI) of the difference was greater than -10%. The 95% CI was calculated with the Wilson score method without continuity correction. AVAXIM 80U Pediatric was non-inferior to HAVRIX 720.

Statistical analysis title	Non-inferiority (Group A - Group B); Adolescents

Statistical analysis description:

Non-inferiority analysis of AVAXIM 80U Pediatric on HAVRIX 720 in adolescents (12 to 15 years) assessed 1 month after booster vaccination.

Comparison groups	Group A; AVAXIM 80U Pediatric v Group B; HAVRIX 720
Number of subjects included in analysis	680
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in AVAXIM 80U Ped.-HAVRIX 720
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.24
upper limit	4.02

Notes:

[4] - The non-inferiority was demonstrated if the lower bound of the two-sided 95% confidence interval (CI) of the difference was greater than -10%. The 95% CI was calculated with the Wilson score method without continuity correction. AVAXIM 80U Pediatric was non-inferior to HAVRIX 720.

Secondary: Geometric Mean Titers (GMTs) of Hepatitis A Antibodies After Primary and Booster Vaccinations with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine

End point title	Geometric Mean Titers (GMTs) of Hepatitis A Antibodies After Primary and Booster Vaccinations with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine

End point description:

Anti-Hepatitis A antibody titers were measured by enzyme-linked immunosorbent assay (ELISA). Geometric mean titers are reported based on age group: Toddlers (12 to 23 months), Children (2 to 11 years), and Adolescents (12 to 15 years).

End point type	Secondary

End point timeframe:

Day 210 (1 month after booster vaccination)

End point values	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	455	227		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
All Subjects; Anti-Hepatitis A antibody titer	2694 (2529.4 to 2869.4)	1525.6 (1369.3 to 1699.7)		
Toddlers; Anti-Hepatitis A antibody titer	3398.6 (2834.7 to 4074.6)	2405.7 (1710.6 to 3383.2)		

Children; Anti-Hepatitis A antibody titer	3029.3 (2750.5 to 3336.4)	1501.4 (1273.6 to 1770)		
Adolescents; Anti-Hepatitis A antibody titer	2142.4 (1984.1 to 2313.3)	1388.2 (1220.8 to 1578.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting Solicited Injection-site Reaction After Any and Each Vaccination with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine

End point title	Percentage of Subjects Reporting Solicited Injection-site Reaction After Any and Each Vaccination with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine

End point description:

Solicited injection site reactions: Tenderness (Toddlers), Pain (Children and Adolescents), Erythema, and Swelling. Grade 3 solicited injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Pain, Incapacitating unable to perform usual activities; Erythema and Swelling > 3 cm.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-any and each injection

End point values	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	239		
Units: Percentage of subjects				
number (not applicable)				
Injection site Tenderness; Post-Any Injection	36.5	40.9		
Grade 3 Injection site Tenderness; Post-Any Inj.	0	0		
Injection site Pain; Post-Any Injection	41.9	41		
Grade 3 Injection site Pain; Post-Any Injection	0	0		
Injection site Erythema; Post-Any Injection	12.1	9.6		
Grade 3 Injection site Erythema; Post-Any Inj.	0	0		
Injection site Swelling; Post-Any Injection	8.8	7.1		
Grade 3 Injection site Swelling; Post-Any Inj.	0	0		
Injection site Tenderness; Post-Injection 1	23.1	31.8		
Grade 3 Injection site Tenderness; Post-Inj. 1	0	0		
Injection site Pain; Post-Injection 1	32.8	29.5		

Grade 3 Injection site Pain; Post-Injection 1	0	0		
Injection site Erythema; Post-Injection 1	6.5	6.3		
Grade 3 Injection site Erythema; Post-Injection 1	0	0		
Injection site Swelling; Post-Injection 1	4.6	5		
Grade 3 Injection site Swelling; Post-Injection 1	0	0		
Injection site Tenderness; Post-Injection 2	23.9	33.3		
Grade 3 Injection site Tenderness; Post-Inj. 2	0	0		
Injection site Pain; Post-Injection 2	23.4	26.4		
Grade 3 Injection site Pain; Post-Injection 2	0	0		
Injection site Erythema; Post-Injection 2	7.4	6.6		
Grade 3 Injection site Erythema; Post-Injection 2	0	0		
Injection site Swelling; Post-Injection 2	5.5	5.2		
Grade 3 Injection site Swelling; Post-Injection 2	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting Solicited Systemic Reaction After Any and Each Vaccination with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine

End point title	Percentage of Subjects Reporting Solicited Systemic Reaction After Any and Each Vaccination with Either AVAXIM™ 80U-Pediatric or HAVRIX 720 Vaccine

End point description:

Solicited systemic reactions (Toddlers; 12 to 23 months of age): Pyrexia (Fever), Vomiting, Abnormal crying, Somnolence (Drowsiness), Anorexia (Loss of appetite), and Irritability. Solicited systemic reactions (Children and Adolescents; 2 to 15 years of age): Pyrexia (Fever), Headache, Malaise, Myalgia.

Grade 3 solicited systemic reactions (Toddlers): Pyrexia, > 39.0°C; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Abnormal crying, > 3 hours; Somnolence, Sleeping most of the time or difficult to wake up; Anorexia, Refuses ≥ 3 feeds/meals or refuses most feeds/meals; Irritability, Inconsolable. Grade 3 solicited systemic reactions (Children and Adolescents): Pyrexia, > 39.0°C; Headache, Malaise, and Myalgia, Prevents daily activities.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-any and each injection

End point values	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	239		
Units: Percentage of subjects				
number (not applicable)				
Fever; Post-Any Injection	27.3	27.6		

Grade 3 Fever; Post-Any Injection	1.3	0.4		
Headache; Post-Any Injection	15	16.1		
Grade 3 Headache; Post-Any Injection	0	0		
Malaise; Post-Any Injection	16.9	18.4		
Grade 3 Malaise; Post-Any Injection	0	0		
Myalgia; Post-Any Injection	25.1	23.5		
Grade 3 Myalgia; Post-Any Injection	0	0		
Vomiting; Post-Any Injection	17.3	9.1		
Grade 3 Vomiting; Post-Any Injection	0	0		
Crying abnormal; Post-Any Injection	26.9	27.3		
Grade 3 Crying abnormal; Post-Any Injection	0	0		
Drowsiness; Post-Any Injection	9.6	4.5		
Grade 3 Drowsiness; Post-Any Injection	0	0		
Appetite lost; Post-Any Injection	25	31.8		
Grade 3 Appetite lost; Post-Any Injection	0	0		
Irritability; Post-Any Injection	25	36.4		
Grade 3 Irritability; Post-Any Injection	0	0		
Fever; Post-Injection 1	18.2	18		
Grade 3 Fever; Post-Injection 1	1	0		
Headache; Post-Injection 1	10.3	13.4		
Grade 3 Headache; Post-Injection 1	0	0		
Malaise; Post-Injection 1	9.6	13.4		
Grade 3 Malaise; Post-Injection 1	0	0		
Myalgia; Post-Injection 1	17.3	16.1		
Grade 3 Myalgia; Post-Injection 1	0	0		
Vomiting; Post-Injection 1	13.5	4.5		
Grade 3 Vomiting; Post-Injection 1	0	0		
Crying abnormal; Post-Injection 1	25	22.7		
Grade 3 Crying abnormal; Post-Injection 1	0	0		
Drowsiness; Post-Injection 1	7.7	0		
Grade 3 Drowsiness; Post-Injection 1	0	0		
Appetite lost; Post-Injection 1	21.2	22.7		
Grade 3 Appetite lost; Post-Injection 1	0	0		
Irritability; Post-Injection 1	23.1	22.7		
Grade 3 Irritability; Post-Injection 1	0	0		
Fever; Post-Injection 2	13.8	13.1		
Grade 3 Fever; Post-Injection 2	0.2	0.4		
Headache; Post-Injection 2	7.1	5.8		
Grade 3 Headache; Post-Injection 2	0	0		
Malaise; Post-Injection 2	8.3	7.7		
Grade 3 Malaise; Post-Injection 2	0	0		
Myalgia; Post-Injection 2	15.6	12		
Grade 3 Myalgia; Post-Injection 2	0	0		
Vomiting; Post-Injection 2	4.3	4.8		
Grade 3 Vomiting; Post-Injection 2	0	0		
Crying abnormal; Post-Injection 2	4.3	9.5		
Grade 3 Crying abnormal; Post-Injection 2	0	0		
Drowsiness; Post-Injection 2	2.2	4.8		
Grade 3 Drowsiness; Post-Injection 2	0	0		

Appetite lost; Post-Injection 2	8.7	9.5		
Grade 3 Appetite lost; Post-Injection 2	0	0		
Irritability; Post-Injection 2	8.7	14.3		
Grade 3 Irritability; Post-Injection 2	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 from Day 0 up to Day 210 (1 month after booster vaccination).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Group A; AVAXIM 80U Pediatric

Reporting group description:

Subjects received AVAXIM 80U Pediatric vaccine at baseline and a booster dose 6 months after the primary injection.

Reporting group title	Group B; HAVRIX 720

Reporting group description:

Subjects received HAVRIX 720 vaccine at baseline and a booster dose 6 months after the primary injection.

Serious adverse events	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 479 (0.84%)	1 / 239 (0.42%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Tonsillitis			
subjects affected / exposed	1 / 479 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
subjects affected / exposed	1 / 479 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scratch by cat			
subjects affected / exposed	1 / 479 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			

subjects affected / exposed	1 / 479 (0.21%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aggravation of bilateral chronic tonsillitis			
subjects affected / exposed	0 / 479 (0.00%)	1 / 239 (0.42%)	
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: 5 %

Non-serious adverse events	Group A; AVAXIM 80U Pediatric	Group B; HAVRIX 720	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	314 / 479 (65.55%)	149 / 239 (62.34%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[1]	64 / 427 (14.99%)	35 / 217 (16.13%)	
occurrences (all)	64	35	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	5 / 52 (9.62%)	1 / 22 (4.55%)	
occurrences (all)	5	1	
General disorders and administration site conditions			
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed[3]	19 / 52 (36.54%)	9 / 22 (40.91%)	
occurrences (all)	19	9	
Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed[4]	179 / 427 (41.92%)	89 / 217 (41.01%)	
occurrences (all)	179	89	
Injection site Erythema			
alternative assessment type: Systematic			

subjects affected / exposed	58 / 479 (12.11%)	23 / 239 (9.62%)	
occurrences (all)	58	23	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	42 / 479 (8.77%)	17 / 239 (7.11%)	
occurrences (all)	42	17	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	131 / 479 (27.35%)	66 / 239 (27.62%)	
occurrences (all)	131	66	
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[5]	72 / 427 (16.86%)	40 / 217 (18.43%)	
occurrences (all)	72	40	
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed[6]	9 / 52 (17.31%)	2 / 22 (9.09%)	
occurrences (all)	9	2	
Psychiatric disorders			
Crying abnormal			
alternative assessment type: Systematic			
subjects affected / exposed[7]	14 / 52 (26.92%)	6 / 22 (27.27%)	
occurrences (all)	14	6	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[8]	13 / 52 (25.00%)	8 / 22 (36.36%)	
occurrences (all)	13	8	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[9]	107 / 427 (25.06%)	51 / 217 (23.50%)	
occurrences (all)	107	51	
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	42 / 479 (8.77%) 42	25 / 239 (10.46%) 25	
Metabolism and nutrition disorders Appetite lost alternative assessment type: Systematic subjects affected / exposed[10] occurrences (all)	13 / 52 (25.00%) 13	7 / 22 (31.82%) 7	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (children and adolescents) for which the diary cards were returned and for which data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (toddlers) for which the diary cards were returned and for which data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (toddlers) for which the diary cards were returned and for which data were available for the event during the period.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (children and adolescents) for which the diary cards were returned and for which data were available for the event during the period.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (children and adolescents) for which the diary cards were returned and for which data were available for the event during the period.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (toddlers) for which the diary cards were returned and for which data were available for the event during the period.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (toddlers) for which the diary cards were returned and for which data were available for the event during the period.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (toddlers) for which the diary cards were returned and for which data were available for the event during the period.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (children and adolescents) for which the diary cards were returned and for which data were available for the event during the period.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days after vaccination; the total number (N) reflects those subjects (toddlers) for which the diary cards were returned and for which data were available for the event during the period.

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