Clinical trial results:
A Phase 2, Randomized, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a Multivalent Pneumococcal Conjugate Vaccine in Healthy Infants

Summary

EudraCT number	2020-003373-21
Trial protocol	Outside EU/EEA
Global end of trial date	11 February 2020

Results information

Result version number	v1 (current)
This version publication date	26 August 2020
First version publication date	26 August 2020

Trial information

Trial identification

Sponsor protocol code	B7471003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03512288
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002330-PIP01-18
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	09 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2020
Global end of trial reached?	Yes
Global end of trial date	11 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile of 20-valent pneumococcal conjugate vaccine (20vPnC) in healthy infants.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 April 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 460
Worldwide total number of subjects	460
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)	460
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled from 16 April 2018 to 11 February 2020 in the United States.

Pre-assignment

Screening details:

A total of 460 subjects of age greater than or equal to (>=) 42 to less than or equal to (<=) 98 days at baseline, were enrolled into the study. Out of these 460 subjects, 458 subjects received study treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	20vPnC

Arm description:

Subjects were randomised to receive a single 0.5 millilitre (mL) intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively).

Arm type	Experimental
Investigational medicinal product name	20-valent pneumococcal conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 20vPnC vaccine intramuscularly into the anterolateral thigh muscle of the left leg at 2, 4, 6, and 12 months of age.

Arm title	13vPnC

Arm description:

Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).

Arm type	Active comparator
Investigational medicinal product name	13-valent pneumococcal conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 13vPnC vaccine intramuscularly into the anterolateral thigh muscle of the left leg at 2, 4, 6, and 12 months of age.

Number of subjects in period 1	20vPnC	13vPnC
Started	232	228
Vaccination 1	231	227
Vaccination 2	222	213
Vaccination 3	210	206
Vaccination 4	197	194
Completed	191	185
Not completed	41	43
Physician decision	-	2
No longer met eligibility criteria	5	2
Medication error without associated adverse event	1	-
Adverse event	1	-
Randomised but not treated	1	1
Unspecified	1	1
Lost to follow-up	12	15
Withdrawal by parent/guardian	14	18
Protocol deviation	6	4

Baseline characteristics

Reporting groups	
Reporting group title	20vPnC
Reporting group description:	
Subjects were randomised to receive a single 0.5 millilitre (mL) intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively).	
Reporting group title	13vPnC
Reporting group description:	
Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).	

Reporting group values	20vPnC	13vPnC	Total
Number of subjects	232	228	460
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)	232	228	460
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: days			
arithmetic mean	64.5	64.5	
standard deviation	± 8.07	± 6.68	-
Gender Categorical Units: Subjects			
Female	112	115	227
Male	120	113	233
Race Units: Subjects			
American Indian or Alaska Native	4	3	7
Asian	9	5	14
Native Hawaiian or Other Pacific Islander	1	3	4
Black or African American	35	29	64
White	161	171	332
More than one race	22	15	37
Unknown or Not Reported	0	2	2
Ethnicity Units: Subjects			
Hispanic/Latino	41	40	81
Non-Hispanic/non-Latino	191	188	379

End points

End points reporting groups

Reporting group title	20vPnC
Reporting group description:	
Subjects were randomised to receive a single 0.5 millilitre (mL) intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively).	
Reporting group title	13vPnC
Reporting group description:	
Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).	

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 1

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 1[1]
End point description:	
Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 centimeter (cm). Redness and swelling were graded as mild (0.5 to 2.0 centimetre [cm]), moderate (greater than [>] 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed " signifies subjects evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Within 7 days after Vaccination 1	

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	224		
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any	24.9 (19.4 to 31.0)	25.4 (19.9 to 31.7)		
Redness: Mild	22.3 (17.1 to 28.2)	23.7 (18.3 to 29.8)		
Redness: Moderate	2.6 (1.0 to 5.6)	1.8 (0.5 to 4.5)		
Redness: Severe	0 (0.0 to 1.6)	0 (0.0 to 1.6)		
Swelling: Any	12.7 (8.6 to 17.7)	14.3 (10.0 to 19.6)		
Swelling: Mild	10.0 (6.5 to 14.7)	12.9 (8.8 to 18.1)		
Swelling: Moderate	2.2 (0.7 to 5.0)	1.3 (0.3 to 3.9)		
Swelling: Severe	0.4 (0.0 to 2.4)	0 (0.0 to 1.6)		

Pain at the injection site: Any	51.1 (44.4 to 57.7)	53.6 (46.8 to 60.2)		
Pain at the injection site: Mild	32.3 (26.3 to 38.8)	35.7 (29.4 to 42.4)		
Pain at the injection site: Moderate	18.3 (13.5 to 24.0)	17.9 (13.1 to 23.5)		
Pain at the injection site: Severe	0.4 (0.0 to 2.4)	0 (0.0 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 2

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 2[2]

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 2

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	204		
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any	24.7 (19.0 to 31.0)	28.4 (22.4 to 35.2)		
Redness: Mild	21.9 (16.5 to 28.0)	24.0 (18.3 to 30.5)		
Redness: Moderate	2.8 (1.0 to 6.0)	4.4 (2.0 to 8.2)		
Redness: Severe	0 (0.0 to 1.7)	0 (0.0 to 1.8)		
Swelling: Any	16.3 (11.6 to 21.9)	18.6 (13.5 to 24.7)		
Swelling: Mild	12.6 (8.4 to 17.7)	13.2 (8.9 to 18.7)		
Swelling: Moderate	3.7 (1.6 to 7.2)	5.4 (2.7 to 9.4)		
Swelling: Severe	0 (0.0 to 1.7)	0 (0.0 to 1.8)		
Pain at the injection site: Any	42.8 (36.1 to 49.7)	48.5 (41.5 to 55.6)		
Pain at the injection site: Mild	26.0 (20.3 to 32.5)	28.9 (22.8 to 35.7)		

Pain at the injection site: Moderate	15.8 (11.2 to 21.4)	19.6 (14.4 to 25.7)		
Pain at the injection site: Severe	0.9 (0.1 to 3.3)	0 (0.0 to 1.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 3

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 3[3]

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 3

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	204		
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any	26.9 (20.9 to 33.6)	26.5 (20.6 to 33.1)		
Redness: Mild	26.4 (20.4 to 33.0)	23.0 (17.4 to 29.4)		
Redness: Moderate	0.5 (0.0 to 2.7)	3.4 (1.4 to 6.9)		
Redness: Severe	0 (0.0 to 1.8)	0 (0.0 to 1.8)		
Swelling: Any	17.9 (12.9 to 23.9)	19.6 (14.4 to 25.7)		
Swelling: Mild	16.9 (12.0 to 22.8)	15.7 (11.0 to 21.4)		
Swelling: Moderate	1.0 (0.1 to 3.5)	3.4 (1.4 to 6.9)		
Swelling: Severe	0 (0.0 to 1.8)	0.5 (0.0 to 2.7)		
Pain at the injection site: Any	44.3 (37.3 to 51.4)	40.7 (33.9 to 47.8)		
Pain at the injection site: Mild	28.9 (22.7 to 35.6)	27.9 (21.9 to 34.6)		
Pain at the injection site: Moderate	14.9 (10.3 to 20.6)	12.7 (8.5 to 18.1)		
Pain at the injection site: Severe	0.5 (0.0 to 2.7)	0 (0.0 to 1.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 4

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Vaccination 4[4]

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 4 safety population included subjects who received Dose 4 and had safety follow up between Dose 4 and 6 months after Dose 4. Here, "number of subjects analyzed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 4

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	185		
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any	25.8 (19.7 to 32.7)	30.3 (23.7 to 37.4)		
Redness: Mild	24.2 (18.2 to 31.0)	25.4 (19.3 to 32.3)		
Redness: Moderate	1.6 (0.3 to 4.6)	4.9 (2.2 to 9.0)		
Redness: Severe	0 (0.0 to 2.0)	0 (0.0 to 2.0)		
Swelling: Any	17.2 (12.1 to 23.4)	14.1 (9.4 to 19.9)		
Swelling: Mild	15.1 (10.2 to 21.0)	12.4 (8.0 to 18.1)		
Swelling: Moderate	2.2 (0.6 to 5.4)	1.6 (0.3 to 4.7)		
Swelling: Severe	0 (0.0 to 2.0)	0 (0.0 to 2.0)		
Pain at the injection site: Any	35.5 (28.6 to 42.8)	35.7 (28.8 to 43.0)		
Pain at the injection site: Mild	26.9 (20.7 to 33.9)	28.6 (22.3 to 35.7)		
Pain at the injection site: Moderate	8.6 (5.0 to 13.6)	7.0 (3.8 to 11.7)		
Pain at the injection site: Severe	0 (0.0 to 2.0)	0 (0.0 to 2.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 1

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 1[5]

End point description:

Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as >=38.0 degree Celsius (C), >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 1

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	224		
Units: percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	14.4 (10.1 to 19.6)	9.8 (6.3 to 14.5)		
Fever: >=38.0 degree C to 38.4 degree C	10.0 (6.5 to 14.7)	6.3 (3.5 to 10.3)		
Fever: >38.4 degree C to 38.9 degree C	3.9 (1.8 to 7.3)	2.2 (0.7 to 5.1)		
Fever: >38.9 degree C to 40.0 degree C	0.4 (0.0 to 2.4)	1.3 (0.3 to 3.9)		
Fever: >40.0 degree C	0 (0.0 to 1.6)	0 (0.0 to 1.6)		
Decreased appetite: Any	25.3 (19.8 to 31.5)	30.4 (24.4 to 36.8)		
Decreased appetite: Mild	16.2 (11.6 to 21.6)	19.2 (14.3 to 25.0)		
Decreased appetite: Moderate	9.2 (5.8 to 13.7)	10.7 (7.0 to 15.5)		
Decreased appetite: Severe	0 (0.0 to 1.6)	0.4 (0.0 to 2.5)		
Drowsiness: Any	68.1 (61.7 to 74.1)	71.0 (64.6 to 76.8)		
Drowsiness: Mild	51.1 (44.4 to 57.7)	54.9 (48.1 to 61.5)		

Drowsiness: Moderate	16.6 (12.0 to 22.1)	14.3 (10.0 to 19.6)		
Drowsiness: Severe	0.4 (0.0 to 2.4)	1.8 (0.5 to 4.5)		
Irritability: Any	79.5 (73.7 to 84.5)	77.7 (71.7 to 83.0)		
Irritability: Mild	23.6 (18.2 to 29.6)	25.9 (20.3 to 32.1)		
Irritability: Moderate	50.7 (44.0 to 57.3)	47.3 (40.6 to 54.1)		
Irritability: Severe	5.2 (2.7 to 9.0)	4.5 (2.2 to 8.1)		
Use of antipyretic or pain medication	38.0 (31.7 to 44.6)	44.2 (37.6 to 51.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 2

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 2[6]

End point description:

Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as >=38.0 degree C, >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 2

Notes:

[6] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	204		
Units: percentage of subjects				
number (confidence interval 95%)				
Fever: >= 38.0 degree C	17.2 (12.4 to 22.9)	23.0 (17.4 to 29.4)		
Fever: >=38.0 degree C to 38.4 degree C	10.2 (6.5 to 15.1)	12.7 (8.5 to 18.1)		
Fever: >38.4 degree C to 38.9 degree C	4.2 (1.9 to 7.8)	7.8 (4.5 to 12.4)		
Fever: >38.9 degree C to 40.0 degree C	2.8 (1.0 to 6.0)	2.5 (0.8 to 5.6)		
Fever: >40.0 degree C	0 (0.0 to 1.7)	0 (0.0 to 1.8)		
Decreased appetite: Any	23.3 (17.8 to 29.5)	27.0 (21.0 to 33.6)		

Decreased appetite: Mild	14.4 (10.0 to 19.8)	14.7 (10.1 to 20.3)		
Decreased appetite: Moderate	7.9 (4.7 to 12.4)	11.8 (7.7 to 17.0)		
Decreased appetite: Severe	0.9 (0.1 to 3.3)	0.5 (0.0 to 2.7)		
Drowsiness: Any	57.2 (50.3 to 63.9)	56.4 (49.3 to 63.3)		
Drowsiness: Mild	37.2 (30.7 to 44.0)	37.7 (31.1 to 44.8)		
Drowsiness: Moderate	17.7 (12.8 to 23.4)	16.7 (11.8 to 22.5)		
Drowsiness: Severe	2.3 (0.8 to 5.3)	2.0 (0.5 to 4.9)		
Irritability: Any	71.2 (64.6 to 77.1)	79.9 (73.7 to 85.2)		
Irritability: Mild	20.0 (14.9 to 26.0)	22.5 (17.0 to 28.9)		
Irritability: Moderate	48.8 (42.0 to 55.7)	52.5 (45.4 to 59.5)		
Irritability: Severe	2.3 (0.8 to 5.3)	4.9 (2.4 to 8.8)		
Use of antipyretic/pain medication	39.5 (33.0 to 46.4)	48.5 (41.5 to 55.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 3

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 3[7]

End point description:

Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as >=38.0 degree C, >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 3

Notes:

[7] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	204		
Units: Percentage of subjects				
number (confidence interval 95%)				

Fever: >=38.0 degree C	17.9 (12.9 to 23.9)	18.1 (13.1 to 24.1)		
Fever: >=38.0 degree C to 38.4 degree C	10.0 (6.2 to 14.9)	9.8 (6.1 to 14.7)		
Fever: >38.4 degree C to 38.9 degree C	4.5 (2.1 to 8.3)	4.9 (2.4 to 8.8)		
Fever: >38.9 degree C to 40.0 degree C	3.5 (1.4 to 7.0)	3.4 (1.4 to 6.9)		
Fever: >40.0 degree C	0 (0.0 to 1.8)	0 (0.0 to 1.8)		
Decreased appetite: Any	30.8 (24.5 to 37.7)	33.3 (26.9 to 40.3)		
Decreased appetite: Mild	20.9 (15.5 to 27.2)	19.1 (14.0 to 25.2)		
Decreased appetite: Moderate	9.5 (5.8 to 14.4)	13.7 (9.3 to 19.2)		
Decreased appetite: Severe	0.5 (0.0 to 2.7)	0.5 (0.0 to 2.7)		
Drowsiness: Any	41.3 (34.4 to 48.4)	45.6 (38.6 to 52.7)		
Drowsiness: Mild	28.9 (22.7 to 35.6)	29.9 (23.7 to 36.7)		
Drowsiness: Moderate	11.4 (7.4 to 16.7)	15.7 (11.0 to 21.4)		
Drowsiness: Severe	1.0 (0.1 to 3.5)	0 (0.0 to 1.8)		
Irritability: Any	72.6 (65.9 to 78.7)	69.6 (62.8 to 75.8)		
Irritability: Mild	28.9 (22.7 to 35.6)	27.5 (21.5 to 34.1)		
Irritability: Moderate	40.8 (33.9 to 47.9)	37.7 (31.1 to 44.8)		
Irritability: Severe	3.0 (1.1 to 6.4)	4.4 (2.0 to 8.2)		
Use of antipyretic/pain medication	42.8 (35.8 to 49.9)	47.1 (40.1 to 54.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 4

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Vaccination 4[8]

End point description:

Systemic events included fever, decreased appetite, drowsiness, irritability and were recorded by using an electronic diary. Fever was categorised as >=38.0 degree C, >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabled, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable; crying could not be comforted). Dose 4 safety population included subjects who received Dose 4 and had safety follow up between Dose 4 and 6 months after Dose 4. Here, "number of subjects analysed" signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after Vaccination 4

Notes:

[8] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	185		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0°C	12.4 (8.0 to 18.0)	14.6 (9.8 to 20.5)		
Fever: >=38.0°C to 38.4°C	5.9 (3.0 to 10.3)	4.3 (1.9 to 8.3)		
Fever: >38.4°C to 38.9°C	3.2 (1.2 to 6.9)	7.0 (3.8 to 11.7)		
Fever: >38.9°C to 40.0°C	3.2 (1.2 to 6.9)	3.2 (1.2 to 6.9)		
Fever: >40.0°C	0 (0.0 to 2.0)	0 (0.0 to 2.0)		
Decreased appetite: Any	23.7 (17.7 to 30.4)	29.2 (22.8 to 36.3)		
Decreased appetite: Mild	13.4 (8.9 to 19.2)	15.7 (10.8 to 21.7)		
Decreased appetite: Moderate	10.2 (6.3 to 15.5)	13.5 (8.9 to 19.3)		
Decreased appetite: Severe	0 (0.0 to 2.0)	0 (0.0 to 2.0)		
Drowsiness: Any	32.8 (26.1 to 40.0)	37.3 (30.3 to 44.7)		
Drowsiness: Mild	26.9 (20.7 to 33.9)	25.4 (19.3 to 32.3)		
Drowsiness: Moderate	4.8 (2.2 to 9.0)	11.9 (7.6 to 17.4)		
Drowsiness: Severe	1.1 (0.1 to 3.8)	0 (0.0 to 2.0)		
Irritability: Any	62.4 (55.0 to 69.3)	62.7 (55.3 to 69.7)		
Irritability: Mild	23.7 (17.7 to 30.4)	19.5 (14.0 to 25.9)		
Irritability: Moderate	36.0 (29.1 to 43.4)	40.0 (32.9 to 47.4)		
Irritability: Severe	2.7 (0.9 to 6.2)	3.2 (1.2 to 6.9)		
Use of antipyretic/pain medication	37.1 (30.1 to 44.5)	44.3 (37.0 to 51.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) From Vaccination 1 to 1 Month After Vaccination 3

End point title	Percentage of Subjects With Adverse Events (AEs) From Vaccination 1 to 1 Month After Vaccination 3[9]

End point description:

An AE was any untoward medical occurrence in study subjects who received study vaccine without regard to possibility of causal relationship. Dose 1 to Dose 3 safety population included subjects who received Dose 1 and had safety follow up between Dose 1 and the blood draw visit 1 month after Dose 3.

End point type	Primary

End point timeframe:

From Vaccination 1 to 1 month after Vaccination 3

Notes:

[9] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	227		
Units: percentage of subjects				
number (confidence interval 95%)	61.0 (54.4 to 67.4)	56.4 (49.7 to 62.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) 1 Month After Vaccination 4

End point title	Percentage of Subjects With Adverse Events (AEs) 1 Month After Vaccination 4[10]

End point description:

An AE was any untoward medical occurrence in study subjects who received study vaccine without regard to possibility of causal relationship. Dose 4 safety population included subjects who received Dose 4 and had safety follow up between Dose 4 and 6 months after Dose 4.

End point type	Primary

End point timeframe:

1 month after Vaccination 4

Notes:

[10] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	194		
Units: percentage of subjects				
number (confidence interval 95%)	18.3 (13.1 to 24.4)	25.3 (19.3 to 32.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Vaccination 1 to 6 Months Following Vaccination 4

End point title	Percentage of Subjects With Serious Adverse Events (SAEs)

	From Vaccination 1 to 6 Months Following Vaccination 4[11]

End point description:

An SAE is any untoward medical occurrence at any dose that results in death; is life-threatening (immediate risk of death); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); results in congenital anomaly/birth defect. Overall safety analysis set included all subjects who received at least 1 dose of study vaccine (20vPnC or 13vPnC) and had safety follow up in the study.

End point type	Primary

End point timeframe:

Vaccination 1 to 6 months after Vaccination 4

Notes:

[11] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	227		
Units: percentage of subjects				
number (confidence interval 95%)	5.2 (2.7 to 8.9)	2.2 (0.7 to 5.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Vaccination 1 to 6 Months Following Vaccination 4

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Vaccination 1 to 6 Months Following Vaccination 4[12]

End point description:

An NDCMC is defined as a disease or medical condition, not previously identified, that is expected to be persistent or is otherwise long-lasting in its effects. Overall safety analysis set included all subjects who received at least 1 dose of study vaccine (20vPnC or 13vPnC) and had safety follow up in the study.

End point type	Primary

End point timeframe:

Vaccination 1 to 6 months after Vaccination 4

Notes:

[12] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	227		
Units: percentage of subjects				
number (confidence interval 95%)	5.2 (2.7 to 8.9)	3.5 (1.5 to 6.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 3

End point title	Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 3

End point description:

Pneumococcal IgG antibody against each of the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F) was measured centrally using direct binding Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding confidence intervals (CIs) based on the Student t distribution. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on dose 1, received assigned vaccine, had valid determinate IgG concentration for at least 1 serotype 1 month post dose 3, had blood collection within 27-56 days post dose 3, had not received prohibited vaccines before the blood draw at 1 month post dose 3, had no major protocol deviations.

End point type	Secondary

End point timeframe:

1 month after Vaccination 3

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	187		
Units: microgram per millilitre				
geometric mean (confidence interval 95%)				
Serotype 1	0.92 (0.81 to 1.05)	1.16 (1.00 to 1.33)		
Serotype 3	0.43 (0.38 to 0.48)	0.56 (0.49 to 0.64)		
Serotype 4	1.36 (1.16 to 1.61)	1.64 (1.39 to 1.93)		
Serotype 5	0.93 (0.79 to 1.11)	1.13 (0.96 to 1.34)		
Serotype 6A	2.28 (1.94 to 2.67)	2.57 (2.16 to 3.05)		
Serotype 6B	0.63 (0.49 to 0.80)	0.99 (0.77 to 1.27)		
Serotype 7F	2.15 (1.92 to 2.40)	2.59 (2.28 to 2.93)		
Serotype 9V	1.22 (1.05 to 1.42)	1.45 (1.24 to 1.70)		
Serotype 14	3.15 (2.69 to 3.70)	3.60 (3.07 to 4.21)		
Serotype 18C	1.59 (1.37 to 1.84)	2.05 (1.76 to 2.38)		
Serotype 19A	0.85 (0.74 to 0.96)	1.02 (0.89 to 1.17)		
Serotype 19F	1.98 (1.76 to 2.22)	2.28 (1.99 to 2.61)		
Serotype 23F	0.94 (0.78 to 1.14)	1.26 (1.03 to 1.55)		
Serotype 8	2.09 (1.90 to 2.30)	0.04 (0.03 to 0.04)		

Serotype 10A	1.67 (1.35 to 2.08)	0.03 (0.03 to 0.03)		
Serotype 11A	1.94 (1.70 to 2.21)	0.01 (0.01 to 0.01)		
Serotype 12F	0.86 (0.72 to 1.01)	0.02 (0.02 to 0.02)		
Serotype 15B	5.86 (5.11 to 6.72)	0.04 (0.04 to 0.05)		
Serotype 22F	4.62 (3.99 to 5.35)	0.01 (0.01 to 0.01)		
Serotype 33F	2.21 (1.87 to 2.61)	0.05 (0.04 to 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 4

End point title	Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 1 Month After Vaccination 4

End point description:

Pneumococcal IgG antibody against each of the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F) was measured centrally using direct binding Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student t distribution. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on dose 1, received assigned vaccine as randomized for all 4 doses, with Dose 4 received in the defined window (365-386 days of age), had valid determinate IgG concentration for at least 1 serotype 1 month post dose 4, had blood collection within 27-56 days post dose 4, had not received prohibited vaccines before the blood draw at 1 month post dose 4, had no major protocol deviations.

End point type	Secondary

End point timeframe:

1 Month after Vaccination 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	166		
Units: microgram per millilitre				
geometric mean (confidence interval 95%)				
Serotype 1	2.65 (2.33 to 3.02)	3.63 (3.20 to 4.11)		
Serotype 3	1.15 (0.97 to 1.35)	1.49 (1.28 to 1.74)		
Serotype 4	7.16 (6.22 to 8.24)	9.45 (8.16 to 10.95)		
Serotype 5	3.41 (2.95 to 3.93)	4.95 (4.29 to 5.71)		
Serotype 6A	13.77 (12.16 to 15.59)	18.83 (16.39 to 21.63)		
Serotype 6B	6.37 (5.42 to 7.50)	9.73 (8.13 to 11.65)		

Serotype 7F	6.14 (5.51 to 6.83)	9.32 (8.26 to 10.52)		
Serotype 9V	5.52 (4.82 to 6.31)	7.78 (6.77 to 8.95)		
Serotype 14	8.61 (7.32 to 10.12)	11.04 (9.44 to 12.90)		
Serotype 18C	5.58 (4.89 to 6.36)	8.46 (7.25 to 9.88)		
Serotype 19A	5.71 (4.91 to 6.64)	7.05 (6.04 to 8.24)		
Serotype 19F	7.79 (6.73 to 9.01)	9.30 (7.99 to 10.83)		
Serotype 23F	6.06 (5.16 to 7.12)	9.81 (8.10 to 11.88)		
Serotype 8	3.12 (2.78 to 3.49)	0.05 (0.04 to 0.06)		
Serotype 10A	9.93 (8.58 to 11.50)	0.03 (0.03 to 0.04)		
Serotype 11A	5.70 (4.96 to 6.54)	0.01 (0.01 to 0.02)		
Serotype 12F	1.92 (1.68 to 2.20)	0.02 (0.02 to 0.03)		
Serotype 15B	18.45 (16.43 to 20.72)	0.04 (0.04 to 0.05)		
Serotype 22F	14.68 (12.62 to 17.08)	0.01 (0.01 to 0.01)		
Serotype 33F	4.70 (4.20 to 5.27)	0.05 (0.04 to 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved Pre-specified Level of Pneumococcal IgG Concentrations Within 1 Month after Vaccination 3

End point title	Percentage of Subjects who Achieved Pre-specified Level of Pneumococcal IgG Concentrations Within 1 Month after Vaccination 3

End point description:

Subjects who achieved pre-specified level of serotypes were reported. Pre-specified levels of serotypes were- for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: >=0.35 microgram per millilitre, for serotype 5: >=0.23 microgram per millilitre, for serotype 6B: >=0.10 microgram per milliliter and for serotype 19A: >=0.12 microgram per millilitre. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on dose 1, received assigned vaccine, had valid determinate IgG concentration for at least 1 serotype 1 month post dose 3, had blood collection within 27-56 days post dose 3, had not received prohibited vaccines before the blood draw at 1 month post dose 3, had no major protocol deviations.

End point type	Secondary

End point timeframe:

1 Month after Vaccination 3

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	187		
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype 1	87.8 (82.3 to 92.1)	87.7 (82.1 to 92.0)		
Serotype 3	65.1 (57.8 to 71.9)	75.4 (68.6 to 81.4)		
Serotype 4	87.8 (82.3 to 92.1)	91.4 (86.5 to 95.0)		
Serotype 5	87.8 (82.3 to 92.1)	89.8 (84.6 to 93.8)		
Serotype 6A	93.7 (89.2 to 96.7)	92.5 (87.8 to 95.8)		
Serotype 6B	86.8 (81.1 to 91.3)	90.4 (85.2 to 94.2)		
Serotype 7F	98.9 (96.2 to 99.9)	97.9 (94.6 to 99.4)		
Serotype 9V	89.4 (84.1 to 93.4)	89.3 (84.0 to 93.3)		
Serotype 14	94.2 (89.8 to 97.1)	95.7 (91.7 to 98.1)		
Serotype 18C	92.6 (87.9 to 95.9)	95.2 (91.1 to 97.8)		
Serotype 19A	98.4 (95.4 to 99.7)	97.9 (94.6 to 99.4)		
Serotype 19F	98.4 (95.4 to 99.7)	96.8 (93.1 to 98.8)		
Serotype 23F	79.9 (73.5 to 85.4)	81.8 (75.5 to 87.1)		
Serotype 8	99.5 (97.1 to 100.0)	3.7 (1.5 to 7.6)		
Serotype 10A	87.8 (82.3 to 92.1)	1.1 (0.1 to 3.8)		
Serotype 11A	97.4 (93.9 to 99.1)	1.6 (0.3 to 4.6)		
Serotype 12F	82.5 (76.4 to 87.7)	0.5 (0.0 to 2.9)		
Serotype 15B	98.9 (96.2 to 99.9)	4.3 (1.9 to 8.3)		
Serotype 22F	98.9 (96.2 to 99.9)	1.1 (0.1 to 3.8)		
Serotype 33F	92.1 (87.2 to 95.5)	1.6 (0.3 to 4.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions and Systemic events: within 7 days after each vaccination (systematic assessment), Non serious AEs: Vaccination 1 to 1 month after Vaccination 3 and Vaccination 4 to 1 month after Vaccination 4, SAEs: up to 16 months after Vaccination 1

Adverse event reporting additional description:

Same event may appear as AE and SAE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Overall safety analysis set was analysed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	20vPnC

Reporting group description:

Subjects were randomised to receive a single 0.5 mL intramuscular injection of 20-valent pneumococcal conjugate vaccine (20vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4 respectively).

Reporting group title	13vPnC

Reporting group description:

Subjects were randomised to receive a single 0.5 mL intramuscular injection of 13-valent pneumococcal conjugate vaccine (13vPnC) at 2, 4, 6, and 12 months of age (Dose/Vaccination 1, 2, 3, and 4, respectively).

Serious adverse events	20vPnC	13vPnC	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 231 (5.19%)	5 / 227 (2.20%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Seizure like phenomena			
subjects affected / exposed	0 / 231 (0.00%)	1 / 227 (0.44%)	
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			
Anaemia			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Respiratory distress			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Oliguria			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 231 (0.43%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	0 / 231 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Meningitis viral			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 231 (0.00%)	1 / 227 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 231 (0.43%)	0 / 227 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	20vPnC	13vPnC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	225 / 231 (97.40%)	224 / 227 (98.68%)	
General disorders and administration site conditions			
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	112 / 231 (48.48%)	120 / 227 (52.86%)	
occurrences (all)	212	225	
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	163 / 231 (70.56%)	167 / 227 (73.57%)	
occurrences (all)	364	368	
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			
subjects affected / exposed	76 / 231 (32.90%)	81 / 227 (35.68%)	
occurrences (all)	132	137	
Pyrexia			
subjects affected / exposed	12 / 231 (5.19%)	10 / 227 (4.41%)	
occurrences (all)	13	12	
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	90 / 231 (38.96%)	90 / 227 (39.65%)	
occurrences (all)	129	133	
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 231 (0.00%)	3 / 227 (1.32%)	
occurrences (all)	0	3	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	9 / 231 (3.90%)	8 / 227 (3.52%)	
occurrences (all)	10	9	
Nasal congestion			
subjects affected / exposed	12 / 231 (5.19%)	7 / 227 (3.08%)	
occurrences (all)	12	7	
Psychiatric disorders			
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	214 / 231 (92.64%)	206 / 227 (90.75%)	
occurrences (all)	597	595	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	6 / 231 (2.60%)	2 / 227 (0.88%)	
occurrences (all)	6	2	
Congenital, familial and genetic disorders			
Plagiocephaly			
subjects affected / exposed	2 / 231 (0.87%)	4 / 227 (1.76%)	
occurrences (all)	2	4	
Nervous system disorders			
Agitation neonatal			
subjects affected / exposed	2 / 231 (0.87%)	4 / 227 (1.76%)	
occurrences (all)	3	5	
Hypersomnia (INCREASED SLEEP)			
alternative assessment type: Systematic			
subjects affected / exposed	188 / 231 (81.39%)	189 / 227 (83.26%)	
occurrences (all)	423	436	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 231 (1.30%)	2 / 227 (0.88%)	
occurrences (all)	3	2	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 231 (4.33%)	6 / 227 (2.64%)	
occurrences (all)	10	6	
Diarrhoea			

subjects affected / exposed	10 / 231 (4.33%)	10 / 227 (4.41%)	
occurrences (all)	11	11	
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 231 (2.60%)	10 / 227 (4.41%)	
occurrences (all)	6	10	
Haematochezia			
subjects affected / exposed	0 / 231 (0.00%)	3 / 227 (1.32%)	
occurrences (all)	0	3	
Teething			
subjects affected / exposed	10 / 231 (4.33%)	16 / 227 (7.05%)	
occurrences (all)	11	17	
Vomiting			
subjects affected / exposed	8 / 231 (3.46%)	9 / 227 (3.96%)	
occurrences (all)	10	9	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	6 / 231 (2.60%)	5 / 227 (2.20%)	
occurrences (all)	6	5	
Dermatitis contact			
subjects affected / exposed	3 / 231 (1.30%)	0 / 227 (0.00%)	
occurrences (all)	3	0	
Dermatitis diaper			
subjects affected / exposed	11 / 231 (4.76%)	8 / 227 (3.52%)	
occurrences (all)	12	8	
Drug eruption			
subjects affected / exposed	1 / 231 (0.43%)	3 / 227 (1.32%)	
occurrences (all)	1	3	
Eczema			
subjects affected / exposed	5 / 231 (2.16%)	3 / 227 (1.32%)	
occurrences (all)	5	3	
Eczema infantile			
subjects affected / exposed	1 / 231 (0.43%)	3 / 227 (1.32%)	
occurrences (all)	1	3	
Rash			
subjects affected / exposed	5 / 231 (2.16%)	5 / 227 (2.20%)	
occurrences (all)	5	5	

Urticaria			
subjects affected / exposed	0 / 231 (0.00%)	4 / 227 (1.76%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Acquired plagiocephaly			
subjects affected / exposed	1 / 231 (0.43%)	4 / 227 (1.76%)	
occurrences (all)	1	4	
Torticollis			
subjects affected / exposed	3 / 231 (1.30%)	2 / 227 (0.88%)	
occurrences (all)	3	2	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	11 / 231 (4.76%)	11 / 227 (4.85%)	
occurrences (all)	11	11	
Candida infection			
subjects affected / exposed	4 / 231 (1.73%)	5 / 227 (2.20%)	
occurrences (all)	4	6	
Candida nappy rash			
subjects affected / exposed	0 / 231 (0.00%)	5 / 227 (2.20%)	
occurrences (all)	0	5	
Cellulitis			
subjects affected / exposed	3 / 231 (1.30%)	1 / 227 (0.44%)	
occurrences (all)	3	1	
Conjunctivitis			
subjects affected / exposed	12 / 231 (5.19%)	11 / 227 (4.85%)	
occurrences (all)	12	11	
Conjunctivitis bacterial			
subjects affected / exposed	3 / 231 (1.30%)	0 / 227 (0.00%)	
occurrences (all)	3	0	
Croup infectious			
subjects affected / exposed	4 / 231 (1.73%)	3 / 227 (1.32%)	
occurrences (all)	4	3	
Ear infection			
subjects affected / exposed	2 / 231 (0.87%)	4 / 227 (1.76%)	
occurrences (all)	2	4	
Gastroenteritis			

subjects affected / exposed	2 / 231 (0.87%)	8 / 227 (3.52%)	
occurrences (all)	2	9	
Gastroenteritis viral			
subjects affected / exposed	6 / 231 (2.60%)	1 / 227 (0.44%)	
occurrences (all)	7	1	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 231 (0.43%)	3 / 227 (1.32%)	
occurrences (all)	1	3	
Nasopharyngitis			
subjects affected / exposed	15 / 231 (6.49%)	16 / 227 (7.05%)	
occurrences (all)	17	18	
Oral candidiasis			
subjects affected / exposed	3 / 231 (1.30%)	3 / 227 (1.32%)	
occurrences (all)	3	4	
Otitis media			
subjects affected / exposed	25 / 231 (10.82%)	21 / 227 (9.25%)	
occurrences (all)	35	27	
Otitis media acute			
subjects affected / exposed	8 / 231 (3.46%)	15 / 227 (6.61%)	
occurrences (all)	8	19	
Pneumonia			
subjects affected / exposed	3 / 231 (1.30%)	0 / 227 (0.00%)	
occurrences (all)	3	0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	2 / 231 (0.87%)	3 / 227 (1.32%)	
occurrences (all)	2	3	
Respiratory tract infection viral			
subjects affected / exposed	6 / 231 (2.60%)	4 / 227 (1.76%)	
occurrences (all)	7	5	
Skin candida			
subjects affected / exposed	0 / 231 (0.00%)	5 / 227 (2.20%)	
occurrences (all)	0	5	
Upper respiratory tract infection			
subjects affected / exposed	40 / 231 (17.32%)	44 / 227 (19.38%)	
occurrences (all)	51	55	

Viral infection			
subjects affected / exposed	10 / 231 (4.33%)	10 / 227 (4.41%)	
occurrences (all)	11	11	
Viral upper respiratory tract infection			
subjects affected / exposed	15 / 231 (6.49%)	11 / 227 (4.85%)	
occurrences (all)	18	11	
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Systematic			
subjects affected / exposed	134 / 231 (58.01%)	136 / 227 (59.91%)	
occurrences (all)	214	245	
Failure to thrive			
subjects affected / exposed	2 / 231 (0.87%)	3 / 227 (1.32%)	
occurrences (all)	2	3	
Feeding disorder			
subjects affected / exposed	2 / 231 (0.87%)	3 / 227 (1.32%)	
occurrences (all)	2	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2018	1. Revised exclusion criteria to <30 days to ensure subjects received the hepatitis B vaccine at less than 30 days of age. 2. Clarified that Pfizer will provide the diphtheria, tetanus, and acellular pertussis (DTaP)-containing vaccine, as antibody levels are assessed in the study. 3. Revised the lower range for moderate severity of injection site redness and swelling from 2.5 cm to >2 .0 cm
11 February 2020	1. Exclusion criterion 5 was updated to "Prior receipt of hepatitis B vaccine at age ≥30 days" to clarify the age of administration and to enable the criterion to be answered with a "yes/no" response.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported