Clinical trial results:
A Phase 3, Randomized, Active-Controlled Trial Evaluating the Safety, Tolerability, and Immunogenicity of a 13-Valent Pneumococcal Conjugate Vaccine (13vPnC) Compared with a 7-Valent Pneumococcal Conjugate Vaccine (7vPnC) in Healthy Infants in China.

Summary

EudraCT number	2014-004953-14
Trial protocol	Outside EU/EEA
Global end of trial date	21 April 2014

Results information

Result version number	v1 (current)
This version publication date	29 June 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	B1851015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01692886
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: 6096A1-3019-CN

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Clinical Trials.gov Call Center, Pfizer Inc., 001 800-718-1021, clinicaltrials.gov_inquiries@pfizer.com
Scientific contact	Clinical Trials.gov Call Center, Pfizer Inc., 001 800-718-1021, clinicaltrials.gov_inquiries@pfizer.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	06 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1)To demonstrate that the immune responses to the 13 pneumococcal serotypes induced by 13vPnC in a 3-, 4-, 5-, and 12-month schedule (Group 2) are non inferior to the immune responses induced by 7vPnC in a 3-, 4-, 5-, and 12-month schedule (Group 1) when measured 1 month after the infant series.
2)To demonstrate that the immune responses to the 13 pneumococcal serotypes induced by 13vPnC in a 2-, 4-, 6-, and 12-month schedule (Group 3) are noninferior to the immune responses induced by 7vPnC in a 3-, 4-, 5-, and 12-month schedule (Group 1) when measured 1 month after the infant series.
3) To evaluate the acceptability of the safety profile of 13vPnC as measured by the incidence rates of local reactions, systemic events, and adverse events (AEs).

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 Conference on Harmonization (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	04 September 2012
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	China: 1674
Worldwide total number of subjects	1674
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)	1674

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:

This phase 3, parallel-group, randomized, active-controlled study randomized 1674 subjects in 5 study centers in China (one coordinating and 4 satellite sites). Subjects were randomized to 1 of 4 groups and were vaccinated with 7vPnC (7-valent pneumococcal conjugate vaccine) or 13vPnC (13-valent pneumococcal conjugate vaccine).

Pre-assignment

Screening details:

Healthy infants (aged 42 to 77 days [approximately 2 months] at the time of enrollment) as determined by medical history, physical examination, and judgment of the investigator were enrolled and vaccinated in this study.

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	Investigator, Carer, Subject, Assessor

Blinding implementation details:

Vaccine allocation for subjects in Groups 1 and 2 were blinded to both the subject’s parent/guardian(s) and the investigator. Vaccine allocations for subjects in Groups 3 and 4 were open to the subject's parent/guardian(s) and the investigator.

Arms

Are arms mutually exclusive?	Yes
Arm title	7vPnC Group 1

Arm description:

Subjects received 7vPnC vaccine administered at 3, 4, 5, and 12 months of age.

Arm type	Active comparator
Investigational medicinal product name	7vPnC
Investigational medicinal product code	
Other name	Prevenar
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received single 0.5 mL (milliliter) of 7vPnC was administered intramuscularly into the anterolateral muscle of the left thigh.

Arm title	13vPnC Group 2

Arm description:

Subjects received 13vPnC vaccine administered at 3, 4, 5, and 12 months of age.

Arm type	Experimental
Investigational medicinal product name	13vPnC
Investigational medicinal product code	
Other name	Prevenar 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received single dose 0.5 mL of 13vPnC was administered intramuscularly into the anterolateral muscle of the left thigh.

Arm title	13vPnC Group 3

Arm description:	
Subjects received 13vPnC vaccine administered at 2, 4, 6, and 12 months of age.	
Arm type	Experimental
Investigational medicinal product name	13vPnC
Investigational medicinal product code	
Other name	Prevenar 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received single 0.5 mL of 13vPnC was administered intramuscularly into the anterolateral muscle of the left thigh.	
Arm title	13vPnC Group 4
Arm description:	
Subjects received 13vPnC vaccine administered at 3, 5, and 12 months of age.	
Arm type	Experimental
Investigational medicinal product name	13vPnC
Investigational medicinal product code	
Other name	Prevenar 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received single dose 0.5 mL of 13vPnC was administered intramuscularly into the anterolateral muscle of the left thigh.	

Number of subjects in period 1	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3
Started	478	478	479
Treated	472	472	476
Completed	417	433	434
Not completed	61	45	45
Consent withdrawn by subject	29	18	19
Does not meet entrance criteria	1	-	1
Protocol violation	-	-	1
Not specified	23	16	10
Adverse event	7	8	7
Lost to follow-up	1	3	7

Number of subjects in period 1	13vPnC Group 4
Started	239
Treated	234
Completed	221
Not completed	18
Consent withdrawn by subject	8
Does not meet entrance criteria	-
Protocol violation	-

Not specified	7
Adverse event	2
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	7vPnC Group 1
Reporting group description:	
Subjects received 7vPnC vaccine administered at 3, 4, 5, and 12 months of age.	
Reporting group title	13vPnC Group 2
Reporting group description:	
Subjects received 13vPnC vaccine administered at 3, 4, 5, and 12 months of age.	
Reporting group title	13vPnC Group 3
Reporting group description:	
Subjects received 13vPnC vaccine administered at 2, 4, 6, and 12 months of age.	
Reporting group title	13vPnC Group 4
Reporting group description:	
Subjects received 13vPnC vaccine administered at 3, 5, and 12 months of age.	

Reporting group values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3
Number of subjects	478	478	479
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	1.97	1.96	2
standard deviation	± 0.343	± 0.339	± 0.334
Gender categorical Units: Subjects			
Female	213	229	226
Male	265	249	253

Reporting group values	13vPnC Group 4	Total	
Number of subjects	239	1674	
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	1.99		
standard deviation	± 0.349	-	
Gender categorical Units: Subjects			
Female	113	781	
Male	126	893	

End points

End points reporting groups

Reporting group title	7vPnC Group 1
Reporting group description:	
Subjects received 7vPnC vaccine administered at 3, 4, 5, and 12 months of age.	
Reporting group title	13vPnC Group 2
Reporting group description:	
Subjects received 13vPnC vaccine administered at 3, 4, 5, and 12 months of age.	
Reporting group title	13vPnC Group 3
Reporting group description:	
Subjects received 13vPnC vaccine administered at 2, 4, 6, and 12 months of age.	
Reporting group title	13vPnC Group 4
Reporting group description:	
Subjects received 13vPnC vaccine administered at 3, 5, and 12 months of age.	

Primary: Percentage of Subjects Achieving a Pneumococcal Immunoglobin G(IgG) Antibody Concentration Greater Than or Equal to (≥)0.35 microgram per milliliter (µg/mL) 1 Month After the Infant Series, 13vPnC Group 2 versus (vs) 7vPnC Group 1

End point title	Percentage of Subjects Achieving a Pneumococcal Immunoglobin G(IgG) Antibody Concentration Greater Than or Equal to (≥)0.35 microgram per milliliter (µg/mL) 1 Month After the Infant Series, 13vPnC Group 2 versus (vs) 7vPnC Group 1[1]

End point description:

The proportion of subjects achieving serotype-specific immunoglobulin G (IgG) concentrations greater than and equal to (≥)0.35 microgram per milliliter (µg/mL) 1 month after the infant series is presented for all common serotypes and 6 additional serotypes. For immunogenicity evaluation, 3 blood samples (approximately 5 mL) were collected during the course of the study. For subjects in Groups 1 and 2, blood samples were collected at the 6-, 12-, and 13-month visits. In the below table 'N' represents the number of subjects with a determinate IgG antibody concentration to the given serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required timeframe, received no prohibited vaccines and had no major protocol deviation.

End point type	Primary

End point timeframe:

1 month after the infant series (6 Months of age)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	446		
Units: Percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=444, 445)	99.8 (98.8 to 100)	100 (99.2 to 100)		
7vPnC - Serotype 6B (N=441, 444)	96.1 (93.9 to 97.7)	93.2 (90.5 to 95.4)		

7vPnC - Serotype 9V (N=446, 445)	99.8 (98.8 to 100)	99.8 (98.8 to 100)		
7vPnC - Serotype 14 (N=446, 445)	100 (99.2 to 100)	99.6 (98.4 to 99.9)		
7vPnC - Serotype 18C (N=446,445)	99.1 (97.7 to 99.8)	98.6 (97.1 to 99.5)		
7vPnC - Serotype 19F (N=445,446)	89.2 (86 to 91.9)	99.8 (98.8 to 100)		
7vPnC - Serotype 23F (N=444,445)	96.8 (94.8 to 98.3)	96.2 (94 to 97.8)		
Additional - Serotype 1 (N=445,444)	1.8 (0.8 to 3.5)	99.5 (98.4 to 99.9)		
Additional - Serotype 3 (N=443, 445)	3.2 (1.7 to 5.2)	99.3 (98 to 99.9)		
Additional - Serotype 5 (N=445, 446)	23.6 (19.7 to 27.8)	99.6 (98.4 to 99.9)		
Additional - Serotype 6A (N=446, 446)	59.9 (55.2 to 64.4)	98.2 (96.5 to 99.2)		
Additional - Serotype 7F (N=445, 445)	4 (2.4 to 6.3)	99.8 (98.8 to 100)		
Additional - Serotype 19A (N=446, 445)	74.4 (70.1 to 78.4)	99.6 (98.4 to 99.9)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4.

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5 percent (%)confidence interval (CI) greater than (>) 0%.

Comparison groups	13vPnC Group 2 v 7vPnC Group 1
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.9
upper limit	1.5

Notes:

[2] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was greater than -10%.

Statistical analysis title	Statistical analysis for 7vPnC -serotype 6B

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Mean difference (final values)
Point estimate	-2.9
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-6.5
upper limit	0.5

Notes:

[3] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was greater than -10%.

Statistical analysis title	Statistical analysis for 7vPnC -serotype 9V

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.3
upper limit	1.3

Notes:

[4] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was greater than -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14.

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.9
upper limit	0.6

Notes:

[5] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was greater than -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C.

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.4
upper limit	1.4

Notes:

[6] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was greater than -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Mean difference (final values)
Point estimate	10.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	7.5
upper limit	14.3

Notes:

[7] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was greater than -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 23F

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.6
upper limit	2.2

Notes:

[8] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was greater than -10%.

Statistical analysis title	Statistical analysis for Additional serotype 1

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	97.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	95.6
upper limit	99

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	96.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	93.6
upper limit	97.9

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	76
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	71.1
upper limit	80.4

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	38.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	32.9
upper limit	43.8

Statistical analysis title	Statistical analysis for Additional serotype 19A
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI > 0%.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	25.1

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	20.6
upper limit	30

Statistical analysis title	Statistical analysis for Additional serotype 7F

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI > 0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	95.7
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	93.1
upper limit	97.6

Primary: Percentage of Subjects achieving a pneumococcal IgG antibody concentration ≥0.35 µg/mL 1 month after the infant series, 13vPnC Group 3 vs 7vPnC Group 1

End point title	Percentage of Subjects achieving a pneumococcal IgG antibody concentration ≥0.35 µg/mL 1 month after the infant series, 13vPnC Group 3 vs 7vPnC Group 1[9]

End point description:

The proportion of subjects achieving serotype-specific IgG concentrations ≥0.35 µg/mL 1 month after the infant series is presented for all common serotypes and 6 additional serotypes. For immunogenicity evaluation, 3 blood samples (approximately 5 mL) were collected during the course of the study. For subjects in Groups 1, blood samples were collected at the 6-, 12-, and 13-month visits. For Group 3 subjects, blood samples were collected at the 7-, 12-, and 13 month visits. In the below table 'N' represents the number of subjects with a determinate IgG antibody concentration to the given serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Primary

End point timeframe:

1 month after the infant series (7 months of age)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	440		
Units: Percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=444, 436)	99.8 (93.9 to 97.7)	100 (98.4 to 99.9)		
7vPnC - Serotype 6B (N=441, 438)	96.1 (98.8 to 100)	94.7 (98.4 to 99.9)		
7vPnC - Serotype 9V (N=446, 440)	99.8 (99.2 to 100)	99.5 (96.7 to 99.4)		
7vPnC - Serotype 14 (N=446, 440)	100 (97.7 to 99.8)	99.5 (96.4 to 99.2)		
7vPnC - Serotype 18C (N=446,440)	99.1 (86 to 91.9)	98.4 (93 to 97.2)		
7vPnC - Serotype 19F (N=438,445)	89.2 (94.8 to 98.3)	98.2 (99.2 to 100)		
7vPnC - Serotype 23F (N=444,438)	96.8 (0.8 to 3.5)	95.4 (95.3 to 98.6)		
Additional - Serotype 1 (N=445, 440)	1.8 (1.7 to 5.2)	100 (97.7 to 99.8)		
Additional - Serotype 3 (N=443, 439)	3.2 (19.7 to 27.8)	97.3 (96.1 to 99.1)		
Additional - Serotype 5 (N=445, 439)	23.6 (55.2 to 64.4)	99.1 (99.2 to 100)		
Additional - Serotype 6A (N=446, 439)	59.9 (98.8 to 100)	97.9 (98 to 99.9)		
Additional - Serotype 7F (N=445, 439)	4 (2.4 to 6.3)	100 (99.2 to 100)		
Additional - Serotype 19A (N=446, 439)	74.4 (70.1 to 78.4)	99.3 (92.2 to 96.6)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.9
upper limit	1.5

Notes:

[10] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was > -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI >0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	Mean difference (final values)
Point estimate	-1.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.7
upper limit	1.8

Notes:

[11] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was > -10%.

Statistical analysis title	Statistical analysis for 7vPnC -serotype 9V

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI >0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.7
upper limit	1.1

Notes:

[12] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was > -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI >0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.9
upper limit	0.7

Notes:

[13] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was > -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.8
upper limit	1.2

Notes:

[14] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was > -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Parameter estimate	Mean difference (final values)
Point estimate	9
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.3
upper limit	12.9

Notes:

[15] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was > -10%.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 23F

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	Mean difference (final values)
Point estimate	-1.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.6
upper limit	1.6

Notes:

[16] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the difference in proportion of responders (13vPnC – 7vPnC) was > -10%.

Statistical analysis title	Statistical analysis for Additional - serotype 1

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	98.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	96.2
upper limit	99.3

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	94.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	91
upper limit	96.4

Statistical analysis title	Statistical analysis for Additional serotype 5

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	13vPnC Group 3 v 7vPnC Group 1
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	75.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	70.6
upper limit	80

Statistical analysis title	Statistical analysis for Additional serotype 6A

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	13vPnC Group 3 v 7vPnC Group 1
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	38.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	32.7
upper limit	43.6

Statistical analysis title	Statistical analysis for Additional- serotype 7F

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	96
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	93.3
upper limit	97.8

Statistical analysis title	Statistical analysis for Additional - serotype 19A

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group. Percentage of responders was statistically significant between the groups if lower bound of 97.5% CI>0%.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	24.9
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	20.3
upper limit	29.8

Primary: Geometric Mean Concentration (GMC) for serotype-specific pneumococcal immunoglobulin G (IgG) antibody 1 month after the infant series, 13vPnC Group 2 vs 7vPnC Group 1

End point title	Geometric Mean Concentration (GMC) for serotype-specific pneumococcal immunoglobulin G (IgG) antibody 1 month after the infant series, 13vPnC Group 2 vs 7vPnC Group 1[17]

End point description:

Antibody GMC for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes (Serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. GMC and corresponding 2-sided 95% CI were evaluated. Geometric means (GMs) were calculated using all subjects with available data for the specified blood draw. In the below table 'N' represents the number of subjects with a determinate antibody concentration for the specified serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Primary

End point timeframe:

1 month after the infant series (6 months of age)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	446		
Units: microgram per milliliter (mcg/mL)				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=444, 445)	15.36 (14.14 to 16.69)	11.96 (11.08 to 12.91)		
7vPnC - Serotype 6B (N=441, 444)	2.88 (2.57 to 3.21)	2.64 (2.35 to 2.96)		
7vPnC - Serotype 9V (N=446, 445)	6.76 (6.28 to 7.27)	5.25 (4.9 to 5.62)		
7vPnC - Serotype 14 (N=446, 445)	17.79 (16.21 to 19.53)	16.36 (14.77 to 18.13)		
7vPnC - Serotype 18C (N=446,444)	6.01 (5.54 to 6.53)	5.71 (5.23 to 6.23)		
7vPnC - Serotype 19F (N=445,446)	5.7 (4.79 to 6.77)	7.4 (6.86 to 7.98)		
7vPnC - Serotype 23F (N=444,445)	4.45 (4.03 to 4.91)	3.97 (3.57 to 4.4)		
Additional - Serotype 1 (N=445,444)	0.01 (0.01 to 0.01)	7.02 (6.44 to 7.65)		
Additional - Serotype 3 (N=443,445)	0.02 (0.02 to 0.02)	4.13 (3.83 to 4.47)		
Additional - Serotype 5 (N=445, 446)	0.23 (0.21 to 0.25)	3.43 (3.18 to 3.7)		
Additional - Serotype 6A (N=446, 446)	0.5 (0.46 to 0.55)	3.8 (3.5 to 4.13)		
Additional - Serotype 7F (N=445, 445)	0.03 (0.03 to 0.03)	7.84 (7.29 to 8.42)		
Additional - Serotype 19A (N=446, 445)	0.57 (0.53 to 0.62)	7.96 (7.28 to 8.7)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	GMC ratio
Point estimate	0.78
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.68
upper limit	0.89

Notes:

[18] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Parameter estimate	GMC ratio
Point estimate	0.92
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.76
upper limit	1.1

Notes:

[19] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	GMC ratio
Point estimate	0.78
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.69
upper limit	0.87

Notes:

[20] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	GMC ratio
Point estimate	0.92
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.79
upper limit	1.08

Notes:

[21] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	GMC ratio
Point estimate	0.95
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.83
upper limit	1.09

Notes:

[22] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
Parameter estimate	GMC ratio
Point estimate	1.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.05
upper limit	1.61

Notes:

[23] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Parameter estimate	GMC ratio
Point estimate	0.89
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.76
upper limit	1.05

Notes:

[24] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for Additional - serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	823.89
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	697.26
upper limit	973.52

Statistical analysis title	Statistical analysis for Additional serotype 3
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	240.05
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	202.16
upper limit	285.05

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	14.93
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	13.15
upper limit	16.95

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	7.54
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	6.54
upper limit	8.69

Statistical analysis title	Statistical analysis for Additional serotype 7F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	256.65
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	217.11
upper limit	303.38

Statistical analysis title	Statistical analysis for Additional - serotype 19A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	13.86
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	12.13
upper limit	15.84

Primary: GMC for serotype-specific pneumococcal IgG antibody 1 month after the infant series, Group 3 vs 7vPnC Group 1

End point title	GMC for serotype-specific pneumococcal IgG antibody 1 month after the infant series, Group 3 vs 7vPnC Group 1[25]

End point description:

Antibody GMC for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes (Serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. GMC and corresponding 2-sided 95% CI were evaluated. GMs were calculated using all subjects with available data for the specified blood draw. In the below table 'N' represents the number of subjects with a determinate antibody concentration for the specified serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required timeframe, received no prohibited vaccines and had no major protocol deviation.

End point type	Primary

End point timeframe:

1 month after the infant series (7 months of age)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	440		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=444,436)	15.36 (14.14 to 16.69)	9.71 (8.97 to 10.52)		
7vPnC - Serotype 6B (N=441, 438)	2.88 (2.57 to 3.21)	3.21 (2.85 to 3.61)		
7vPnC - Serotype 9V (N=446, 440)	6.76 (6.28 to 7.27)	4.27 (3.97 to 4.6)		
7vPnC - Serotype 14 (N=446, 440)	17.79 (16.21 to 19.53)	17.11 (15.44 to 18.96)		
7vPnC - Serotype 18C (N=446, 440)	6.01 (5.54 to 6.53)	5.76 (5.25 to 6.33)		
7vPnC - Serotype 19F (N=445,438)	5.7 (4.79 to 6.77)	6.93 (6.26 to 7.66)		
7vPnC - Serotype 23F (N=444, 438)	4.45 (4.03 to 4.91)	4.02 (3.58 to 4.51)		
Additional - Serotype 1 (N=445, 440)	0.01 (0.01 to 0.01)	7.77 (7.16 to 8.45)		
Additional - Serotype 3 (N=443, 439)	0.02 (0.02 to 0.02)	1.68 (1.56 to 1.82)		
Additional - Serotype 5 (N=445, 439)	0.23 (0.21 to 0.25)	3.61 (3.33 to 3.9)		
Additional - Serotype 6A (N=446, 439)	0.5 (0.46 to 0.55)	4.76 (4.34 to 5.23)		
Additional - Serotype 7F (N=445, 439)	0.03 (0.03 to 0.03)	8.28 (7.7 to 8.91)		
Additional - Serotype 19A (N=446, 439)	0.57 (0.53 to 0.62)	5.1 (4.68 to 5.57)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Parameter estimate	GMC ratio
Point estimate	0.63
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.55
upper limit	0.72

Notes:

[26] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
Parameter estimate	GMC ratio
Point estimate	1.12
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.93
upper limit	1.34

Notes:

[27] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Parameter estimate	GMC ratio
Point estimate	0.63
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.56
upper limit	0.71

Notes:

[28] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
Parameter estimate	GMC ratio
Point estimate	0.96
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.82
upper limit	1.13

Notes:

[29] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Parameter estimate	GMC ratio
Point estimate	0.96
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.83
upper limit	1.1

Notes:

[30] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
Parameter estimate	GMC ratio
Point estimate	1.22
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.97
upper limit	1.53

Notes:

[31] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for 7vPnC serotype 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
Parameter estimate	GMC ratio
Point estimate	0.9
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.76
upper limit	1.08

Notes:

[32] - Noninferiority of 13vPnC in comparison with 7vPnC was assessed with respect to the 7 common serotypes (only). The noninferiority criterion was met for each serotype if the lower limit of the 97.5% CI for the GMC ratio (13vPnC / 7vPnC) was > 0.5.

Statistical analysis title	Statistical analysis for Additional - serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	912.65
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	773.95
upper limit	1076.22

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	97.77
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	82.27
upper limit	116.19

Statistical analysis title	Statistical analysis for Additional - serotype 5

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	15.69
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	13.79
upper limit	17.86

Statistical analysis title	Statistical analysis for Additional - serotype 6A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	9.45
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	8.13
upper limit	10.97

Statistical analysis title	Statistical analysis for Additional - serotype 7F
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	271.28
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	229.23
upper limit	321.04

Statistical analysis title	Statistical analysis for Additional - serotype 19A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 97.5% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	8.89

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	7.8
upper limit	10.14

Primary: Percentage of subjects reporting local reactions within 7 days after dose 1 in infant series

End point title	Percentage of subjects reporting local reactions within 7 days after dose 1 in infant series[33]

End point description:

Following local reactions were assessed: redness, swelling, and tenderness at the site of the pneumococcal conjugate injection. Details of local reactions were collected via e-diary for 7 days after each 13vPnC or 7vPnC vaccination. The below table included following for redness and swelling: Any, Mild (0.5-2.0 centimeters [cm]), Moderate (greater than [>] 2.0-7.0 cm), and Severe (>7.0 cm).For tenderness following are presented: Any, Present, and Significant (present and interfered with limb movement). N = number of subjects reporting yes for at least 1 day or no for all 7 days. Infant series safety population was used after dose 1. The safety analysis set included all subjects who received at least 1 dose of investigational product.

End point type	Primary

End point timeframe:

Within 7 days of dose 1 of infant series

Notes:

[33] - 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 reported for this endpoint.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	13vPnC Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	472[34]	472[35]	476[36]	234[37]
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness - Any (N=470, 472, 472, 233)	4 (2.5 to 6.2)	3.2 (1.8 to 5.2)	5.7 (3.8 to 8.2)	3.4 (1.5 to 6.7)
Redness - Mild (N=470, 472, 472, 233)	4 (2.5 to 6.2)	3.2 (1.8 to 5.2)	5.5 (3.6 to 8)	3.4 (1.5 to 6.7)
Redness - Moderate (N=470, 472, 471, 233)	0.2 (0 to 1.2)	0 (0 to 0.8)	0.6 (0.1 to 1.9)	0 (0 to 1.6)
Redness - Severe (N=470, 472, 471, 233)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 1.6)
Swelling - Any (N=470, 472, 472, 233)	5.5 (3.6 to 8)	4 (2.4 to 6.2)	5.5 (3.6 to 8)	5.6 (3 to 9.4)
Swelling - Mild (N=470, 472, 472, 233)	4.9 (3.1 to 7.3)	3.4 (1.9 to 5.4)	5.1 (3.3 to 7.5)	5.2 (2.7 to 8.8)
Swelling - Moderate (N=470, 472, 471, 233)	1.1 (0.3 to 2.5)	0.6 (0.1 to 1.8)	1.1 (0.3 to 2.5)	0.9 (0.1 to 3.1)
Swelling - Severe (N=470, 472, 471, 233)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 1.6)
Tenderness - Any (N=470, 472, 472, 233)	4.3 (2.6 to 6.5)	3.2 (1.8 to 5.2)	7.6 (5.4 to 10.4)	5.2 (2.7 to 8.8)
Tenderness - Present (N=470, 472, 472, 233)	3.8 (2.3 to 6)	3 (1.6 to 4.9)	7.6 (5.4 to 10.4)	3.9 (1.8 to 7.2)
Tenderness - Significant (N=470, 472, 471, 233)	0.4 (0.1 to 1.5)	0.2 (0 to 1.2)	0 (0 to 0.8)	1.3 (0.3 to 3.7)

Notes:

[34] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

[35] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

[36] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

[37] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects reporting local reactions within 7 days after dose 2 in infant series

End point title	Percentage of subjects reporting local reactions within 7 days after dose 2 in infant series[38]

End point description:

Following local reactions were assessed: redness, swelling, and tenderness at the site of the pneumococcal conjugate injection. Details of local reactions were collected via e-diary for 7 days after each 13vPnC or 7vPnC vaccination. The below table included following for redness and swelling: Any, Mild (0.5-2.0 cm), Moderate (>2.0-7.0 cm), and Severe (>7.0 cm). For tenderness following are presented: Any, Present, and Significant (present and interfered with limb movement). In the below table the section. N = number of subjects reporting yes for at least 1 day or no for all 7 days. Infant series safety population was used after dose 2. The safety analysis set included all subjects who received at least 1 dose of investigational product.

End point type	Primary

End point timeframe:

Within 7 days of dose 2 of infant series

Notes:

[38] - 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 reported for this endpoint.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	13vPnC Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	466[39]	469[40]	467[41]	232[42]
Units: percentage of subjects				
number (confidence interval 95%)				
Redness - Any (N=459, 462, 460, 232)	2.8 (1.5 to 4.8)	2.2 (1 to 3.9)	4.3 (2.7 to 6.6)	1.7 (0.5 to 4.4)
Redness - Mild (N=459, 462, 460, 232)	2.6 (1.4 to 4.5)	1.7 (0.8 to 3.4)	3.9 (2.3 to 6.1)	1.7 (0.5 to 4.4)
Redness - Moderate (N=459, 462, 460, 232)	0.4 (0.1 to 1.6)	0.6 (0.1 to 1.9)	0.7 (0.1 to 1.9)	1.7 (0.5 to 4.4)
Redness - Severe (N=459, 462, 459, 232)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 1.6)
Swelling - Any (N=459, 462, 459, 232)	3.5 (2 to 5.6)	2.4 (1.2 to 4.2)	4.1 (2.5 to 6.4)	1.7 (0.5 to 4.4)
Swelling - Mild (N=459, 462, 459, 232)	3.3 (1.8 to 5.3)	2.2 (1 to 3.9)	3.7 (2.2 to 5.9)	1.7 (0.5 to 4.4)
Swelling - Moderate (N=459, 462, 459, 232)	0.7 (0.1 to 1.9)	0.4 (0.1 to 1.6)	0.4 (0.1 to 1.6)	0.4 (0 to 2.4)
Swelling - Severe (N=459, 462, 459, 232)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 1.6)
Tenderness - Any (N=459, 462, 460, 232)	2.8 (1.5 to 4.8)	2.4 (1.2 to 4.2)	6.1 (4.1 to 8.7)	2.6 (1 to 5.5)
Tenderness - Present (N=459, 462, 460, 232)	2.6 (1.4 to 4.5)	1.9 (0.9 to 3.7)	6.1 (4.1 to 8.7)	2.6 (1 to 5.5)
Tenderness - Significant (N=459, 462, 459, 232)	0.2 (0 to 1.2)	0.4 (0.1 to 1.6)	0 (0 to 0.8)	0 (0 to 1.6)

Notes:

[39] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

[40] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

[41] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

[42] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects reporting local reactions within 7 days after dose 3 in infant series

End point title	Percentage of subjects reporting local reactions within 7 days after dose 3 in infant series[43][44]

End point description:

Following local reactions were assessed: redness, swelling, and tenderness at the site of the pneumococcal conjugate injection. Details of local reactions were collected via e-diary for 7 days after each 13vPnC or 7vPnC vaccination. The below table included following for redness and swelling: Any, Mild (0.5-2.0 cm), Moderate (>2.0-7.0 cm), and Severe (>7.0 cm).For tenderness following are presented: Any, Present, and Significant (present and interfered with limb movement). In the below table, N = number of subjects reporting yes for at least 1 day or no for all 7 days. Infant series safety population was used after dose 3. The safety analysis set included all subjects who received at least 1 dose of investigational product.

End point type	Primary

End point timeframe:

Within 7 days of dose 3 of infant series

Notes:

[43] - 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 reported for this endpoint.

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	463	467	460	
Units: percentage of subjects				
number (confidence interval 95%)				
Redness -Any (N=463, 467, 460)	1.9 (0.9 to 3.7)	2.1 (1 to 3.9)	1.7 (0.8 to 3.4)	
Redness- Mild (N=463, 467, 460)	1.7 (0.7 to 3.4)	2.1 (1 to 3.9)	1.1 (0.4 to 2.5)	
Redness- Moderate (N=463, 467, 460)	0.2 (0 to 1.2)	0.2 (0 to 1.2)	0.9 (0.2 to 2.2)	
Redness- Severe (N= 463, 467, 460)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	
Swelling- Any (463, 467, 460)	1.9 (0.9 to 3.7)	1.9 (0.9 to 3.6)	2.4 (1.2 to 4.2)	
Swelling -Mild (N=463, 467, 460)	1.9 (0.9 to 3.7)	1.9 (0.9 to 3.6)	2.2 (1 to 4)	
Swelling -Moderate (N=463, 467, 460)	0 (0 to 0.8)	0.2 (0 to 1.2)	0.7 (0.1 to 1.9)	
Swelling -Severe (N= 463, 467, 460)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	
Tenderness-Any (463, 467, 460)	5 (3.2 to 7.4)	3.4 (2 to 5.5)	3.5 (2 to 5.6)	
Tenderness- Present (N=463, 467, 460)	4.3 (2.7 to 6.6)	3.2 (1.8 to 5.2)	3.3 (1.8 to 5.3)	
Tenderness-Significant (N=463, 467, 460)	0.6 (0.1 to 1.9)	0.2 (0 to 1.2)	0.2 (0 to 1.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects reporting systemic events and antipyretic medication use within 7 days after dose 1 in infant series

End point title	Percentage of subjects reporting systemic events and antipyretic medication use within 7 days after dose 1 in infant series[45]

End point description:

Following systemic events were assessed: decreased appetite, irritability, increased sleep, decreased sleep, fever, and use of antipyretic medication to treat or prevent symptoms. N = number of subjects reporting yes for at least 1 day or no for all 7 days. Infant series safety population was used after dose 1. The safety analysis set included all subjects who received at least 1 dose of investigational product.

End point type	Primary

End point timeframe:

Within 7 days after dose 1 of infant series

Notes:

[45] - 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 reported for this endpoint.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	13vPnC Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	472[46]	472[47]	476[48]	234[49]
Units: percentage of subjects				
number (confidence interval 95%)				
Temperature ≥38 degree (°)C (N=470, 472, 472, 233)	0.6 (0.1 to 1.9)	1.1 (0.3 to 2.5)	1.7 (0.7 to 3.3)	1.3 (0.3 to 3.7)
Temperature ≥38°C but ≤39°C (N=470, 472, 472, 233)	0.6 (0.1 to 1.9)	1.1 (0.3 to 2.5)	1.7 (0.7 to 3.3)	1.3 (0.3 to 3.7)
Temperature >39°C but ≤40°C (N=470, 472, 471, 233)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 1.6)
Temperature >40°C (N=470, 472, 471, 233)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 1.6)
Decreased appetite (N=470, 472, 471, 233)	4.3 (2.6 to 6.5)	1.9 (0.9 to 3.6)	4.7 (3 to 7)	1.7 (0.5 to 4.3)
Irritability (N=470, 472, 472, 233)	4.7 (3 to 7)	3.4 (1.9 to 5.4)	12.3 (9.5 to 15.6)	4.3 (2.1 to 7.8)
Increased sleep (N=470, 472, 471, 233)	2.6 (1.3 to 4.4)	0.6 (0.1 to 1.8)	7.4 (5.2 to 10.2)	0.9 (0.1 to 3.1)
Decreased sleep (N=470, 472, 471, 233)	2.8 (1.5 to 4.7)	1.9 (0.9 to 3.6)	5.7 (3.8 to 8.2)	2.6 (1 to 5.5)
Antipyretic medication use (N=470, 472, 473, 233)	1.7 (0.7 to 3.3)	1.5 (0.6 to 3)	2.7 (1.5 to 4.7)	3 (1.2 to 6.1)

Notes:

[46] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

[47] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

[48] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

[49] - Analysed subjects includes the number of subjects who received dose 1 vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects reporting systemic events and antipyretic medication use within 7 days after dose 2 in infant series

End point title	Percentage of subjects reporting systemic events and antipyretic medication use within 7 days after dose 2 in infant series[50]

End point description:

Following systemic events were assessed: decreased appetite, irritability, increased sleep, decreased sleep, fever, and use of antipyretic medication to treat or prevent symptoms. N = number of subjects reporting yes for at least 1 day or no for all 7 days.Infant series safety population was used after dose 2. The safety analysis set included all subjects who received at least 1 dose of investigational product.

End point type	Primary

End point timeframe:

7 days after dose 2 of infant series

Notes:

[50] - 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 reported for this endpoint.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	13vPnC Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	466[51]	469[52]	467[53]	232[54]
Units: Percentage of subjects				
number (confidence interval 95%)				
Temperature ≥38°C (N=459, 462, 459, 232)	0.9 (0.2 to 2.2)	1.5 (0.6 to 3.1)	1.7 (0.8 to 3.4)	1.3 (0.3 to 3.7)
Temperature ≥38°C but ≤39°C (N=459, 462, 459, 232)	0.9 (3.6 to 7.9)	1.5 (0.6 to 3.1)	1.7 (0.8 to 3.4)	1.3 (0.3 to 3.7)
Temperature >39°C but ≤40°C (N=459, 462, 459, 232)	0 (0.1 to 1.9)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 1.6)
Temperature >40°C (N=459, 462, 459, 232)	0 (0.8 to 3.4)	0 (1.2 to 4.2)	0 (0 to 0.8)	0 (0 to 1.6)
Decreased appetite (N=459, 462, 459, 232)	2.6 (0.6 to 3.1)	1.9 (0 to 0.8)	2 (0.9 to 3.7)	0.4 (0 to 2.4)
Irritability (N=459, 462, 460, 232)	5.4 (0.2 to 2.2)	3.7 (0.9 to 3.7)	3.3 (1.8 to 5.3)	0.9 (0.1 to 3.1)
Increased sleep (N=459, 462, 459, 232)	0.7 (0 to 0.8)	0 (2.2 to 5.8)	0.2 (0 to 1.2)	0.4 (0 to 2.4)
Decreased sleep (N=459, 462, 459, 232)	1.7 (0 to 0.8)	1.7 (0 to 0.8)	1.3 (0.5 to 2.8)	0 (0 to 1.6)
Antipyretic medication use (N=459, 462, 459, 232)	1.5 (1.4 to 4.5)	2.4 (0.8 to 3.4)	2 (0.9 to 3.7)	0.9 (0.1 to 3.1)

Notes:

[51] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

[52] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

[53] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

[54] - Analysed subjects includes the number of subjects who received dose 2 vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects reporting systemic events and antipyretic medication use within 7 days after dose 3 in infant series

End point title	Percentage of subjects reporting systemic events and antipyretic medication use within 7 days after dose 3 in infant series[55][56]

End point description:

Following systemic events were assessed: decreased appetite, irritability, increased sleep, decreased sleep, fever, and use of antipyretic medication to treat or prevent symptoms. N = number of subjects reporting yes for at least 1 day or no for all 7 days. Infant series safety population was used after dose 3. The safety analysis set included all subjects who received at least 1 dose of investigational product.

End point type	Primary

End point timeframe:

7 days after dose 3 of infant series

Notes:

[55] - 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 reported for this endpoint.

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	462[57]	467[58]	464[59]	
Units: Percentage of subjects				
number (confidence interval 95%)				
Temperature ≥38°C (N=463, 467, 460)	1.7 (0.7 to 3.4)	2.1 (1 to 3.9)	1.7 (0.8 to 3.4)	
Temperature ≥38°C but ≤39°C (N=463, 467, 460)	1.5 (0.6 to 3.1)	1.9 (0.9 to 3.6)	1.7 (0.8 to 3.4)	
Temperature >39°C but ≤40°C (N=463, 467, 460)	0.2 (0 to 1.2)	0.2 (0 to 1.2)	0.2 (0 to 1.2)	
Temperature >40°C (N=463, 467, 460)	0 (0 to 0.8)	0 (0 to 0.8)	0 (0 to 0.8)	
Decreased appetite (N=463, 467, 460)	2.4 (1.2 to 4.2)	1.3 (0.5 to 2.8)	2.4 (1.2 to 4.2)	
Irritability (N=463, 467, 460)	2.4 (1.2 to 4.2)	2.1 (1 to 3.9)	4.3 (2.7 to 6.6)	
Increased sleep (N=463, 467, 460)	0.6 (0.1 to 1.9)	0.4 (0.1 to 1.5)	0.4 (0.1 to 1.6)	
Decreased sleep (N=463, 467, 460)	0.2 (0 to 1.2)	0.9 (0.2 to 2.2)	1.3 (0.5 to 2.8)	
Antipyretic medication use (N=463, 467, 460)	2.2 (1 to 3.9)	1.7 (0.7 to 3.3)	3 (1.7 to 5.1)	

Notes:

[57] - Analysed subjects includes the number of subjects who received dose 3 vaccination.

[58] - Analysed subjects includes the number of subjects who received dose 3 vaccination.

[59] - Analysed subjects includes the number of subjects who received dose 3 vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects reporting local reactions within 7 days after toddler dose

End point title	Percentage of subjects reporting local reactions within 7 days after toddler dose[60]

End point description:

Following local reactions were assessed: redness, swelling, and tenderness at the site of the pneumococcal conjugate injection. Details of local reactions were collected via e-diary for 7 days after each 13vPnC or 7vPnC vaccination. The below table included following for redness and swelling: Any, Mild (0.5-2.0 cm), Moderate (>2.0-7.0 cm), and Severe (>7.0 cm).For tenderness following are presented: Any, Present, and Significant (present and interfered with limb movement).N = number of subjects reporting yes for at least 1 day or no for all 7 days. The safety analysis set after toddler dose was used. Safety analysis set included all subjects who received at least 1 dose of investigational product.

End point type	Primary

End point timeframe:

Within 7 days of toddler dose vaccination

Notes:

[60] - 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 reported for this endpoint.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	13vPnC Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	436[61]	447[62]	448[63]	225[64]
Units: percentage of subjects				
number (confidence interval 95%)				
Redness - Any (N=432, 447, 446, 225)	2.1 (1 to 3.9)	3.4 (1.9 to 5.5)	3.6 (2.1 to 5.8)	1.8 (0.5 to 4.5)
Redness - Mild (N=432, 447, 446, 225)	1.4 (0.5 to 3)	2.5 (1.2 to 4.4)	2.5 (1.2 to 4.4)	0.4 (0 to 2.5)
Redness - Moderate (N=432, 447, 446, 225)	1.4 (0.5 to 3)	1.6 (0.6 to 3.2)	1.3 (0.5 to 2.9)	1.3 (0.3 to 3.8)
Redness - Severe (N=432, 447, 446, 225)	0 (0 to 0.9)	0 (0 to 0.8)	0 (0 to 0.8)	0.4 (0 to 2.5)
Swelling - Any (N=432, 447, 446, 225)	3.5 (2 to 5.7)	3.6 (2.1 to 5.7)	3.6 (2.1 to 5.8)	3.1 (1.3 to 6.3)
Swelling - Mild (N=432, 447, 446, 225)	2.3 (1.1 to 4.2)	2.7 (1.4 to 4.6)	2.7 (1.4 to 4.7)	1.8 (0.5 to 4.5)
Swelling - Moderate (N=432, 447, 446, 225)	1.6 (0.7 to 3.3)	1.3 (0.5 to 2.9)	1.3 (0.5 to 2.9)	1.8 (0.5 to 4.5)
Swelling - Severe (N=432, 447, 446, 225)	0 (0 to 0.9)	0 (0 to 0.8)	0 (0 to 0.8)	0.4 (0 to 2.5)
Tenderness - Any (N=432, 447, 446, 225)	6.5 (4.3 to 9.2)	4.9 (3.1 to 7.4)	5.4 (3.5 to 7.9)	5.3 (2.8 to 9.1)
Tenderness - Present (N=432, 447, 446, 225)	6.5 (4.3 to 9.2)	4.5 (2.8 to 6.8)	4.7 (2.9 to 7.1)	5.3 (2.8 to 9.1)
Tenderness - Significant (N=432, 447, 446, 225)	0 (0 to 0.9)	0.4 (0.1 to 1.6)	0.7 (0.1 to 2)	0 (0 to 1.6)

Notes:

[61] - Analysed subjects includes the number of subjects who received toddler dose.

[62] - Analysed subjects includes the number of subjects who received toddler dose.

[63] - Analysed subjects includes the number of subjects who received toddler dose.

[64] - Analysed subjects includes the number of subjects who received toddler dose.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects reporting systemic events and antipyretic medication use within 7 days after toddler dose

End point title	Percentage of Subjects reporting systemic events and antipyretic medication use within 7 days after toddler dose[65]

End point description:

Following systemic events were assessed: decreased appetite,irritability, increased sleep, decreased sleep, fever, and use of antipyretic medication to treat or prevent symptoms. N = number of subjects

reporting yes for at least 1 day or no for all 7 days.

End point type	Primary

End point timeframe:

within 7 days of toddler dose vaccination

Notes:

[65] - 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 reported for this endpoint.

End point values	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3	13vPnC Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	436[66]	447[67]	448[68]	225[69]
Units: Percentage of subjects				
number (confidence interval 95%)				
Temperature ≥38°C (N=432, 447, 446, 225)	3.2 (0.8 to 5.4)	6.7 (4.6 to 9.4)	6.7 (4.6 to 9.5)	6.2 (3.4 to 10.2)
Temperature ≥38°C but ≤39°C (N=432, 447, 446, 225)	3.2 (1.8 to 5.4)	6.5 (4.4 to 9.2)	6.3 (4.2 to 8.9)	6.2 (3.4 to 10.2)
Temperature >39°C but ≤40°C (N=432, 447, 446, 225)	0.2 (0 to 1.3)	0.9 (0.2 to 2.3)	0.4 (0.1 to 1.6)	0 (0 to 1.6)
Temperature >40°C (N=432, 447, 446, 225)	0 (0 to 0.9)	0.2 (0 to 1.2)	0 (0 to 0.8)	0 (0 to 1.6)
Decreased appetite (N=433, 447, 446, 225)	3.5 (2 to 5.6)	2.5 (1.2 to 4.4)	2.5 (1.2 to 4.4)	2.2 (0.7 to 5.1)
Irritability (N=432, 447, 446, 225)	4.4 (2.7 to 6.8)	3.4 (1.9 to 5.5)	3.6 (2.1 to 5.8)	3.1 (1.3 to 6.3)
Increased sleep (N=432, 447, 446, 225)	0.7 (0.1 to 2)	0 (0 to 0.8)	0 (0 to 0.8)	0.4 (0 to 2.5)
Decreased sleep (N=432, 447, 446, 225)	1.6 (0.7 to 3.3)	2.2 (1.1 to 4.1)	1.6 (0.6 to 3.2)	0.9 (0.1 to 3.2)
Antipyretic medication use (N=432, 447, 446, 225)	5.3 (3.4 to 7.9)	5.4 (3.5 to 7.9)	5.4 (3.5 to 7.9)	4.4 (2.2 to 8)

Notes:

[66] - Analysed subjects includes the number of subjects who received toddler dose.

[67] - Analysed subjects includes the number of subjects who received toddler dose.

[68] - Analysed subjects includes the number of subjects who received toddler dose.

[69] - Analysed subjects includes the number of subjects who received toddler dose.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects achieving a pneumococcal IgG antibody concentration ≥0.35 µg/mL 1 month after the infant series, 13vPnC Group 4 vs 7vPnC Group 1

End point title	Percentage of Subjects achieving a pneumococcal IgG antibody concentration ≥0.35 µg/mL 1 month after the infant series, 13vPnC Group 4 vs 7vPnC Group 1[70]

End point description:

The proportion of subjects achieving serotype-specific IgG concentrations ≥0.35 µg/mL 1 month after the infant series is presented for all common serotypes and 6 additional serotypes. For immunogenicity evaluation, 3 blood samples (approximately 5 mL) were collected during the course of the study. For subjects in Groups 1, blood samples were collected at the 6-, 12-, and 13-month visits. For Group 4 subjects, blood samples were collected at the 6-, 12-, and 13 month visits. In the below table 'N' represents the number of subjects with a determinate IgG antibody concentration to the given serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the infant series (6 months of age)

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	224		
Units: percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=444,224)	99.8 (98.8 to 100)	99.6 (97.5 to 100)		
7vPnC - Serotype 6B (N=441,224)	96.1 (93.9 to 97.7)	70.1 (63.6 to 76)		
7vPnC - Serotype 9V (N= 446, 224)	99.8 (98.8 to 100)	98.2 (95.5 to 99.5)		
7vPnC - Serotype 14 (N= 446,223)	100 (99.2 to 100)	99.1 (96.8 to 99.9)		
7vPnC - Serotype 18C (N= 446, 223)	99.1 (97.7 to 99.8)	95.5 (91.9 to 97.8)		
7vPnC - Serotype 19F (N= 445, 224)	89.2 (86 to 91.9)	98.7 (96.1 to 99.7)		
7vPnC - Serotype 23F (N= 444, 224)	96.8 (94.8 to 98.3)	90.6 (86 to 94.1)		
Additional - Serotype 1 (N= 445,224)	1.8 (0.8 to 3.5)	100 (98.4 to 100)		
Additional - Serotype 3 (N= 443, 224)	3.2 (1.7 to 5.2)	99.6 (97.5 to 100)		
Additional - Serotype 5 (N= 445, 224)	23.6 (19.7 to 27.8)	98.2 (95.5 to 99.5)		
Additional - Serotype 6A (N=446, 223)	59.9 (55.2 to 64.4)	97.3 (94.2 to 99)		
Additional - Serotype 7F (N=445, 224)	4 (2.4 to 6.3)	100 (98.4 to 100)		
Additional - Serotype 19A (N= 446, 224)	74.4 (70.1 to 78.4)	98.4 (96.1 to 99.7)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	1

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	-26.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.6
upper limit	-19.9

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	-0.1

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	0.1

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	-0.7

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	9.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.9
upper limit	12.9

Statistical analysis title	Statistical analysis for 7vPnC - serotype 23F
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.9
upper limit	-2.2

Statistical analysis title	Statistical analysis for Additional - serotype 1
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	98.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	96.5
upper limit	99.3

Statistical analysis title	Statistical analysis for Additional - serotype 3
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	96.4

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	93.9
upper limit	97.9

Statistical analysis title	Statistical analysis for Additional - serotype 5
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	74.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	70
upper limit	78.7

Statistical analysis title	Statistical analysis for Additional - serotype 7F
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	96
Confidence interval	
level	95 %
sides	2-sided
lower limit	93.7
upper limit	97.6

Statistical analysis title	Statistical analysis for Additional - serotype 6A
Statistical analysis description:	
Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	37.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	32.3
upper limit	42.5

Statistical analysis title	Statistical analysis for Additional - serotype 19A

Statistical analysis description:

Difference in proportions, 13vPnC-7vPnC reference, expressed as percentage. The reference value is the corresponding proportion in 7vPnC group.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	24.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.9
upper limit	28.7

Secondary: GMC for serotype-specific pneumococcal IgG antibody 1 month after the infant series, 13vPnC Group 4 vs 7vPnC Group 1

End point title	GMC for serotype-specific pneumococcal IgG antibody 1 month after the infant series, 13vPnC Group 4 vs 7vPnC Group 1[71]

End point description:

Antibody GMC for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes (Serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. GMC and corresponding 2-sided 95% CI were evaluated. GMs were calculated using all subjects with available data for the specified blood draw. In the below table 'N' represents the number of subjects with a determinate antibody concentration for the specified serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the infant series (6 months of age)

Notes:

[71] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	224		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N= 444,224)	15.36 (2.57 to 13.21)	8.68 (7.62 to 9.88)		
7vPnC - Serotype 6B (N= 441,224)	2.88 (6.28 to 7.27)	0.74 (0.62 to 0.89)		
7vPnC - Serotype 9V (N= 446,224)	6.76 (16.21 to 19.53)	4.42 (3.88 to 5.04)		
7vPnC - Serotype 14 (N= 446,223)	17.79 (14.14 to 16.69)	10.75 (8.99 to 12.87)		
7vPnC - Serotype 18C (N= 446,223)	6.01 (5.54 to 6.53)	4.17 (3.6 to 4.84)		
7vPnC - Serotype 19F (N= 445, 224)	5.7 (4.79 to 6.77)	10.64 (9 to 12.59)		
7vPnC - Serotype 23F (N=444, 224)	4.45 (4.03 to 4.91)	2.29 (1.9 to 2.77)		
Additional - Serotype 1 (N= 445,224)	0.01 (0.01 to 0.01)	6.98 (6.2 to 7.85)		
Additional - Serotype 3 (N= 443, 224)	0.02 (0.02 to 0.02)	2.59 (2.32 to 2.9)		
Additional - Serotype 5 (N= 445, 224)	0.23 (0.21 to 0.25)	3.19 (2.82 to 3.61)		
Additional - Serotype 6A (N= 446,223)	0.5 (0.46 to 0.55)	4.18 (3.62 to 4.83)		
Additional - Serotype 7F (N= 445,224)	0.03 (0.03 to 0.03)	8.12 (7.26 to 9.07)		
Additional - Serotype 19A (N=446, 224)	0.57 (0.53 to 0.62)	6.41 (5.44 to 7.54)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.66

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.32

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.75

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.5
upper limit	0.73

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.81

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.87
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.42
upper limit	2.45

Statistical analysis title	Statistical analysis for 7vPnC serotype 23F
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.63

Statistical analysis title	Statistical analysis for Additional - serotype 1
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	818.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	680.02
upper limit	985.99

Statistical analysis title	Statistical analysis for Additional - serotype 3
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	150.7
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	123.61
upper limit	183.73

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	13.89
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	12.03
upper limit	16.03

Statistical analysis title	Statistical analysis for Additional serotype 6A

Statistical analysis description:

CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	8.29
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	7.02
upper limit	9.78

Statistical analysis title	Statistical analysis for Additional- serotype 7F

Statistical analysis description:

CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	265.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	218.6
upper limit	323.51

Statistical analysis title	Statistical analysis for Additional - serotype 19A

Statistical analysis description:

CI for the ratio are back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (13vPnC-7vPnC reference).

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	11.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.55
upper limit	13.06

Secondary: Percentage of Subjects achieving a pneumococcal Opsonophagocytic Activity (OPA) antibody titer ≥ Lower Limit of Quantitation (LLOQ) in infant series, 13vPnC Group 2 vs 7vPnC Group 1

End point title	Percentage of Subjects achieving a pneumococcal Opsonophagocytic Activity (OPA) antibody titer ≥ Lower Limit of Quantitation (LLOQ) in infant series, 13vPnC Group 2 vs 7vPnC Group 1[72]

End point description:

A randomly selected subset was analyzed for serum OPA elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1 and 2, blood samples (approximately 5 mL) were collected at the 6-, 12-, and 13-month visits. In the below table 'N' indicates the number of subjects with a determinate postinfant series OPA antibody titer to the given serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the infant series (6 Months of age)

Notes:

[72] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	446		
Units: percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=112, 111)	100 (21.2 to 39.2)	100 (96.7 to 100)		
7vPnC - Serotype 6B (N=114, 111)	97.4 (96.8 to 100)	99.1 (96.7 to 100)		
7vPnC - Serotype 9V (N=110, 110)	97.3 (92.2 to 99.4)	97.3 (96.8 to 100)		
7vPnC - Serotype 14 (N=110, 111)	100 (92.2 to 99.4)	100 (93.6 to 99.8)		

7vPnC - Serotype 18C (N=111, 111)	100 (96.7 to 100)	100 (96.7 to 100)		
7vPnC - Serotype 19F (N=107, 110)	97.2 (96.7 to 100)	97.2 (95.1 to 100)		
7vPnC - Serotype 23F (N=110, 111)	97.3 (92.2 to 99.4)	97.3 (92.2 to 99.4)		
Additional - Serotype 1 (N=112, 111)	0 (92.2 to 99.4)	95.5 (96.7 to 100)		
Additional - Serotype 3 (N=115, 115)	5.2 (0 to 3.2)	100 (96.7 to 100)		
Additional - Serotype 5 (N=113, 112)	0.9 (1.9 to 11)	98.2 (92.2 to 99.4)		
Additional - Serotype 6A (N=105, 110)	83.8 (0 to 4.8)	100 (92.2 to 99.4)		
Additional - Serotype 7F (N=102, 113)	6.9 (75.3 to 90.3)	100 (89.8 to 98.5)		
Additional - Serotype 19A (N=108, 110)	29.6 (2.8 to 13.6)	98.2 (96.8 to 100)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	6.6

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	5.3

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	3.4

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	3.3

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	7.1

Statistical analysis title	Statistical analysis for 7vPnC serotype 23F

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	6.9

Statistical analysis title	Statistical analysis for Additional - serotype 1

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	13vPnC Group 2 v 7vPnC Group 1
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	95.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	89.8
upper limit	98.5

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	94.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	89
upper limit	98.1

Statistical analysis title	Statistical analysis for Additional serotype 5

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	97.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	92.3
upper limit	99.4

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	16.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.7
upper limit	24.7

Statistical analysis title	Statistical analysis for Additional- serotype 7F
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	93.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	86.4
upper limit	97.2

Statistical analysis title	Statistical analysis for Additional - serotype 19A
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	68.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	58.8
upper limit	77.1

Secondary: Percentage of Subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ in infant series, 13vPnC Group 3 vs 7vPnC Group 1

End point title	Percentage of Subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ in infant series, 13vPnC Group 3 vs 7vPnC Group 1[73]

End point description:

A randomly selected subset was analyzed for serum OPA elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F,
9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1, blood samples were collected at the 6-, 12-, and 13-month
visits. For Group 3 subjects, blood samples were collected at the 7-, 12-, and 13 month visits. In the below table 'N' indicates the number of subjects with a determinate postinfant series OPA antibody titer to the given serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the infant series (7 months of age)

Notes:

[73] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	440		
Units: percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=112, 100)	100 (96.8 to 100)	100 (96.4 to 100)		
7vPnC - Serotype 6B (N=114, 101)	97.4 (92.5 to 99.5)	98 (93 to 99.8)		
7vPnC - Serotype 9V (N=110, 99)	97.3 (92.2 to 99.4)	97 (91.4 to 99.4)		
7vPnC - Serotype 14 (N=110, 96)	100 (96.7 to 100)	100 (96.2 to 100)		
7vPnC - Serotype 18C (N=111,98)	100 (96.7 to 100)	100 (96.3 to 100)		
7vPnC - Serotype 19F (N=107, 97)	97.2 (92 to 99.4)	99 (94.4 to 100)		
7vPnC - Serotype 23F (N=110,98)	97.3 (92.2 to 99.4)	96.9 (91.3 to 99.4)		
Additional - Serotype 1 (N=112, 98)	0 (0 to 3.2)	96.9 (91.3 to 99.4)		
Additional - Serotype 3 (N=115, 102)	5.2 (1.9 to 11)	100 (96.4 to 100)		

Additional - Serotype 5 (N=113, 101)	0.9 (0 to 4.8)	95 (88.8 to 98.4)		
Additional - Serotype 6A (N=105,97)	83.8 (75.3 to 90.3)	99 (94.4 to 100)		
Additional - Serotype 7F (N=102, 100)	6.9 (2.8 to 13.6)	100 (96.4 to 100)		
Additional - Serotype 19A (N=108,98)	29.6 (21.2 to 39.2)	98 (92.8 to 99.8)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3.3

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	5.8

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC	

reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	5.1

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	3.4

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3.4

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	7.1

Statistical analysis title	Statistical analysis for 7vPnC serotype 23F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	5.1

Statistical analysis title	Statistical analysis for Additional - serotype 1
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	96.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	91.3
upper limit	99.4

Statistical analysis title	Statistical analysis for Additional serotype 3
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	94.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	89
upper limit	98.1

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	94.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	87.7
upper limit	97.8

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	15.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	7.4
upper limit	23.6

Statistical analysis title	Statistical analysis for Additional- serotype 7F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	93.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	86.4
upper limit	97.2

Statistical analysis title	Statistical analysis for Additional - serotype 19A
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	68.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.5
upper limit	77.1

Secondary: Percentage of subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ in infant series, 13vPnC Group 4 vs 7vPnC Group 1

End point title	Percentage of subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ in infant series, 13vPnC Group 4 vs 7vPnC Group 1[74]

End point description:

A randomly selected subset was analyzed for serum OPA elicited by the 13 pneumococcal serotypes (1,

3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1, blood samples were collected at the 6-, 12-, and 13-month visits. For Group 4 subjects, blood samples were collected at the 6-, 12-, and 13 month visits. In the below table 'N' indicates the number of subjects with a determinate postinfant series OPA antibody titer to the given serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the infant series (7 months of age)

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	224		
Units: percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=112, 101)	100 (96.8 to 100)	99 (94.6 to 100)		
7vPnC - Serotype 6B (N=114, 99)	97.4 (92.5 to 99.5)	79.8 (70.5 to 87.2)		
7vPnC - Serotype 9V (N=110,99)	97.3 (92.2 to 99.4)	90.9 (83.4 to 95.8)		
7vPnC - Serotype 14 (N=110, 101)	100 (96.7 to 100)	100 (96.4 to 100)		
7vPnC - Serotype 18C (N=111,103)	100 (96.7 to 100)	99 (94.7 to 100)		
7vPnC - Serotype 19F (N=107,98)	97.2 (92 to 99.4)	99 (94.4 to 100)		
7vPnC - Serotype 23F (N=110,102)	97.3 (92.2 to 99.4)	98 (93.1 to 99.8)		
Additional - Serotype 1 (N=112, 102)	0 (0 to 3.2)	95.1 (88.9 to 98.4)		
Additional - Serotype 3 (N=115, 107)	5.2 (1.9 to 11)	100 (96.6 to 100)		
Additional - Serotype 5 (N=113, 104)	0.9 (0 to 4.8)	98.1 (93.2 to 99.8)		
Additional - Serotype 6A (N=105, 102)	83.8 (75.3 to 90.3)	100 (96.4 to 100)		
Additional - Serotype 7F (N=102, 104)	6.9 (2.8 to 13.6)	100 (96.4 to 100)		
Additional - Serotype 19A (N=108, 102)	29.6 (21.2 to 39.2)	95.1 (88.9 to 98.4)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	2.3

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	0.1

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-17.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.9
upper limit	-8.7

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3.3

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	2.4

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	7.1

Statistical analysis title	Statistical analysis for 7vPnC serotype 23F
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	6.1

Statistical analysis title	Statistical analysis for Additional - serotype 1
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	13vPnC Group 4 v 7vPnC Group 1
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	95.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	88.9
upper limit	98.4

Statistical analysis title	Statistical analysis for Additional serotype 3
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	94.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	89
upper limit	98.1

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	16.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.7
upper limit	24.7

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	97.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	92.1
upper limit	99.4

Statistical analysis title	Statistical analysis for Additional- serotype 7F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	93.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	86.4
upper limit	97.2

Statistical analysis title	Statistical analysis for Additional - serotype 19A

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	65.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	55
upper limit	74.7

Secondary: Serotype-specific OPA Geometric Mean Titer (GMT) 1 month after the infant series 13vPnC Group 2 vs 7vPnC Group 1

End point title	Serotype-specific OPA Geometric Mean Titer (GMT) 1 month after the infant series 13vPnC Group 2 vs 7vPnC Group 1[75]

End point description:

A randomly selected subset was analyzed for serum OPA GMT elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1 and 2, blood samples (approximately 5 mL) were collected at the 6-, 12-, and 13-month visits. In the below table 'N' represents the number of subjects with a determinate antibody titer for the specified serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the infant series (6 months of age)

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	446		
Units: GMT				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=112, 111)	4650 (3890.2 to 7011.5)	4266 (3499.9 to 5198.8)		
7vPnC - Serotype 6B (N=114, 111)	3725 (3804.6 to 5682.5)	3471 (2736 to 4402.5)		
7vPnC - Serotype 9V (N=110, 110)	2727 (2834.3 to 4894.7)	2502 (1914 to 3270.1)		
7vPnC - Serotype 14 (N=110, 111)	4301 (2097.7 to 3544.5)	3391 (2724.7 to 4221.2)		
7vPnC - Serotype 18C (N=111, 111)	8548 (3544.8 to 5219.1)	8223 (6999.1 to 9661)		
7vPnC - Serotype 19F (N=107, 110)	889 (7293.5 to 10017.2)	1561 (1264 to 1927.6)		
7vPnC - Serotype 23F (N=110, 111)	5223 (698.5 to 1130.2)	4992 (3931.4 to 6337.5)		
Additional - Serotype 1 (N=112, 111)	4 (-99999 to 99999)	98 (79.6 to 121.8)		
Additional - Serotype 3 (N=115, 115)	5 (4.1 to 5)	339 (300.7 to 382.6)		
Additional - Serotype 5 (N=113, 112)	4 (3.9 to 4.2)	218 (183.4 to 260.3)		
Additional - Serotype 6A (N=105, 110)	491 (309.4 to 778.7)	4230 (3457 to 5175.3)		
Additional - Serotype 7F (N=102, 113)	6 (4.4 to 7.3)	3622 (3218.7 to 4075.7)		
Additional - Serotype 19A (N=108, 110)	11 (8 to 15.5)	644 (512 to 810.4)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.21

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.34

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.05

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.33

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.2

Statistical analysis title	Statistical analysis for 7vPnC serotype 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.39

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	2.41

Statistical analysis title	Statistical analysis for Additional - serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	24.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.95
upper limit	30.39

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	75.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	63.9
upper limit	88.19

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	53.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	44.81
upper limit	63.96

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	8.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.26
upper limit	14.11

Statistical analysis title	Statistical analysis for Additional - serotype 19A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	57.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	38.85
upper limit	85.87

Statistical analysis title	Statistical analysis for Additional- serotype 7F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	642.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	491.58
upper limit	839.53

Secondary: Serotype-specific OPA GMT 1 month after the infant series 13vPnC Group 3 vs 7vPnC Group 1

End point title	Serotype-specific OPA GMT 1 month after the infant series 13vPnC Group 3 vs 7vPnC Group 1[76]

End point description:

A randomly selected subset was analyzed for serum OPA GMT elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1, blood samples were collected at the 6-, 12-, and 13- month visits. For Group 3 subjects, blood samples were collected at the 7-, 12-, and 13 month visits. In the below table 'N' represents the number of subjects with a determinate antibody titer for the specified serotype. Evaluable infant pneumococcal immunogenicity population included participants aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation. Here 99999 and -99999 in 95 percent (%) Confidence interval signifies not estimable.

End point type	Secondary

End point timeframe:

1 month after the infant series (7 months of age)

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	440		
Units: GMT				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=112, 110)	4650 (3804.6 to 5682.5)	3470 (2767.3 to 4350.3)		
7vPnC - Serotype 6B (N=114, 101)	3725 (2834.3 to 4894.7)	2402 (1778.5 to 3244.1)		
7vPnC - Serotype 9V (N=110,99)	2727 (2097.7 to 3544.5)	2294 (1695.6 to 3103.2)		
7vPnC - Serotype 14 (N=110, 96)	4301 (3544.8 to 5219.1)	2288 (1783.6 to 2935.5)		
7vPnC - Serotype 18C (N=111,98)	8548 (7293.5 to 10017.2)	8692 (7071.3 to 10684.3)		
7vPnC - Serotype 19F (N=107,97)	889 (698.5 to 1130.2)	1087 (855.6 to 1382.2)		
7vPnC - Serotype 23F (N=110,98)	5223 (3890.2 to 7011.5)	3608 (2608.1 to 4990.3)		
Additional - Serotype 1 (N=112, 98)	4 (-99999 to 99999)	132 (103.8 to 166.7)		
Additional - Serotype 3 (N=114, 102)	5 (4.1 to 5)	209 (180.6 to 241.1)		
Additional - Serotype 5 (N=113, 101)	4 (3.9 to 4.2)	234 (184.5 to 297.2)		
Additional - Serotype 6A (N=105,97)	491 (309.4 to 778.7)	3518 (2781.7 to 4450)		
Additional - Serotype 7F (N=102, 100)	6 (4.4 to 7.3)	4164 (3591 to 4828.9)		
Additional - Serotype 19A (N=108,98)	11 (8 to 15.5)	529 (407.7 to 687.3)		

Statistical analyses

Statistical analysis title	Statistical analysis for 7vPnC - serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.01

Statistical analysis title	Statistical analysis for 7vPnC - serotype 6B
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	0.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.43
upper limit	0.96

Statistical analysis title	Statistical analysis for 7vPnC - serotype 9V
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.25

Statistical analysis title	Statistical analysis for 7vPnC - serotype 14
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.72

Statistical analysis title	Statistical analysis for 7vPnC - serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.31

Statistical analysis title	Statistical analysis for 7vPnC - serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	13vPnC Group 3 v 7vPnC Group 1
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.72

Statistical analysis title	Statistical analysis for 7vPnC serotype 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.07

Statistical analysis title	Statistical analysis for Additional - serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	32.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.38
upper limit	40.97

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	46.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	38.7
upper limit	55.14

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	57.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	45.69
upper limit	72.05

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.23
upper limit	12.15

Statistical analysis title	Statistical analysis for Additional- serotype 7F
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	738.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	551.83
upper limit	988.55

Statistical analysis title	Statistical analysis for Additional- Serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	13vPnC Group 3 v 7vPnC Group 1
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	47.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.13
upper limit	72.38

Secondary: Serotype-specific OPA GMT 1 month after the infant series 13vPnC Group 4 vs 7vPnC Group 1

End point title	Serotype-specific OPA GMT 1 month after the infant series 13vPnC Group 4 vs 7vPnC Group 1[77]

End point description:

A randomly selected subset was analyzed for serum OPA GMT elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Group 1, blood samples were collected at the 6-, 12-, and 13- month visits. For Group 4 subjects, blood samples were collected at the 6-, 12-, and 13 month visits. In the below table 'N' represents the number of subjects with a determinate antibody titer for the specified serotype. Evaluable infant pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after infant series within the required time frame, received no prohibited vaccines and had no major protocol deviation. Here 99999 and -99999 in the confidence interval signifies not estimable.

End point type	Secondary

End point timeframe:

1 month after the infant series (6 months of age)

Notes:

[77] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	224		
Units: GMT				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=112, 101)	4650 (3804.6 to 5682.5)	3546 (2726.6 to 4611.9)		
7vPnC - Serotype 6B (N=114,99)	3725 (2834.3 to 4894.7)	452 (269.7 to 756.9)		
7vPnC - Serotype 9V (N=110,99)	2727 (2097.7 to 3544.5)	1439 (945 to 2191.5)		
7vPnC - Serotype 14 (N=110, 101)	4301 (3544.8 to 5219.1)	3101 (2436.8 to 3945.2)		
7vPnC - Serotype 18C (N=111,103)	8548 (7293.5 to 10017.2)	4742 (3715.6 to 6052.4)		
7vPnC - Serotype 19F (N=107,98)	889 (698.5 to 1130.2)	1283 (999.3 to 1646.8)		
7vPnC - Serotype 23F (N=110,102)	5223 (3890.2 to 7011.5)	2708 (1917.4 to 3825.4)		
Additional - Serotype 1 (N=112,95)	4 (-99999 to 99999)	95 (75.7 to 118.5)		
Additional - Serotype 3 (N=115,107)	5 (4.1 to 5)	268 (232.9 to 308.8)		
Additional - Serotype 5 (N=113, 104)	4 (3.9 to 4.2)	203 (164.4 to 249.6)		
Additional - Serotype 6A (N=105, 102)	491 (309.4 to 778.7)	2486 (1978.1 to 3124.2)		
Additional - Serotype 7F (N=102, 104)	6 (4.4 to 7.3)	3527 (3054.8 to 4072.8)		
Additional - Serotype 19A (N=108, 102)	11 (8 to 15.5)	447 (327.1 to 611.6)		

Statistical analyses

Statistical analysis title	Statistical analysis for Serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.06

Statistical analysis title	Statistical analysis for Serotype 6B
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.21

Statistical analysis title	Statistical analysis for Serotype 9V
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.85

Statistical analysis title	Statistical analysis for Serotype 14
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.98

Statistical analysis title	Statistical analysis for Serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.74

Statistical analysis title	Statistical analysis for Serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	2.04

Statistical analysis title	Statistical analysis for Serotypec 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.81

Statistical analysis title	Statistical analysis for Additional serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	23.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.15
upper limit	29.27

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	59.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	49.81
upper limit	70.74

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.02
upper limit	8.49

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	49.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	40.49
upper limit	60.81

Statistical analysis title	Statistical analysis for Additional serotype 19A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	40.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.54
upper limit	62.98

Statistical analysis title	Statistical analysis for Additional serotype 7F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	625.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	469.5
upper limit	833.19

Secondary: GMC for serotype-specific pneumococcal IgG antibody 1 month after the toddler dose, 13vPnC Group 2 vs 7vPnC Group 1

End point title	GMC for serotype-specific pneumococcal IgG antibody 1 month after the toddler dose, 13vPnC Group 2 vs 7vPnC Group 1[78]

End point description:

Antibody GMC for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes (Serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. GMC and corresponding 2-sided 95% CIs were evaluated. GMs were calculated using all subjects with available data for the specified blood draw. In the below table 'N' represents the number of subjects with a determinate antibody concentration for the specified serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	409		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=399,409)	14.88 (13.64 to 16.25)	12.75 (11.64 to 13.96)		
7vPnC - Serotype 6B (N=399, 409)	11.94 (10.82 to 13.18)	11.64 (10.46 to 12.95)		
7vPnC - Serotype 9V (N=399, 409,)	8.36 (7.7 to 9.08)	6.79 (6.24 to 7.38)		
7vPnC - Serotype 14 (N= 399,409)	24.55 (22.71 to 26.55)	21.79 (20.13 to 23.6)		
7vPnC - Serotype 18C (N=399, 409)	9.02 (8.29 to 9.82)	8.96 (8.22 to 9.76)		
7vPnC - Serotype 19F (N=399, 409)	11.36 (10.36 to 12.46)	18.02 (16.48 to 19.7)		
7vPnC - Serotype 23F (N=399, 409)	12.61 (11.34 to 14.03)	12.15 (10.82 to 13.65)		
Additional - Serotype 1 (N=347,409)	0.06 (0.05 to 0.07)	11.77 (10.62 to 13.03)		
Additional - Serotype 3 (N=347,409)	0.14 (0.12 to 0.16)	1.73 (1.62 to 1.85)		
Additional - Serotype 5 (N= 398,409)	0.67 (0.61 to 0.74)	8.05 (7.4 to 8.75)		
Additional - Serotype 6A (N=399,409)	3.02 (2.68 to 3.4)	11.21 (10.18 to 12.35)		
Additional - Serotype 7F (N=394,409)	0.1 (0.08 to 0.12)	9.73 (8.92 to 10.61)		
Additional - Serotype 19A (N=399,409)	2.48 (2.27 to 2.7)	15.27 (13.99 to 16.67)		

Statistical analyses

Statistical analysis title	Statistical analysis for Serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.97

Statistical analysis title	Statistical analysis for Serotype 6B

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.13

Statistical analysis title	Statistical analysis for Serotype 9V

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.91

Statistical analysis title	Statistical analysis for Serotype 14

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.99

Statistical analysis title	Statistical analysis for Serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.12

Statistical analysis title	Statistical analysis for Serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.39
upper limit	1.8

Statistical analysis title	Statistical analysis for Serotype 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.13

Statistical analysis title	Statistical analysis for additional Serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	200.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	160.75
upper limit	251.28

Statistical analysis title	Statistical analysis for additional Serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	12.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.58
upper limit	14.12

Statistical analysis title	Statistical analysis for additional Serotype 5

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	11.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.54
upper limit	13.62

Statistical analysis title	Statistical analysis for additional Serotype 6A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	13vPnC Group 2 v 7vPnC Group 1
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	3.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.19
upper limit	4.32

Statistical analysis title	Statistical analysis for additional Serotype 7F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	96.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	80.28
upper limit	117.04

Statistical analysis title	Statistical analysis for additional Serotype 19A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	6.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.4
upper limit	6.97

Secondary: GMC for serotype-specific pneumococcal IgG antibody 1 month after the toddler dose, 13vPnC Group 3 vs 7vPnC Group 1

End point title	GMC for serotype-specific pneumococcal IgG antibody 1 month after the toddler dose, 13vPnC Group 3 vs 7vPnC Group 1[79]

End point description:

Antibody GMC for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes (Serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. GMC and corresponding 2-sided 95% CIs were evaluated. GMs were calculated using all subjects with available data for the specified blood draw. In the below table 'N' represents the number of subjects with a determinate antibody concentration for the specified serotype.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	423		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=399,423)	14.88 (13.64 to 16.25)	13.25 (12.19 to 14.4)		
7vPnC - Serotype 6B (N=399,423)	11.94 (10.82 to 13.18)	13.05 (11.88 to 14.35)		
7vPnC - Serotype 9V (N=399,423)	8.36 (7.7 to 9.08)	7.04 (6.48 to 7.65)		
7vPnC - Serotype 14 (N=423,399)	24.55 (22.71 to 26.55)	20.61 (19.04 to 22.31)		
7vPnC - Serotype 18C (N=423,399)	9.02 (8.29 to 9.82)	11.38 (10.49 to 12.34)		
7vPnC - Serotype 19F (N=399,423)	11.36 (10.36 to 12.46)	15.96 (14.57 to 17.47)		
7vPnC - Serotype 23F (N=399,423)	12.61 (11.34 to 14.03)	13.9 (12.42 to 15.55)		
Additional - Serotype 1 (N=423,347)	0.06 (0.05 to 0.07)	11.86 (10.84 to 12.98)		
Additional - Serotype 3 (N=370, 421)	0.14 (0.12 to 0.16)	1.41 (1.33 to 1.5)		
Additional - Serotype 5 (N=423, 398)	0.67 (0.61 to 0.74)	8.27 (7.62 to 8.97)		
Additional - Serotype 6A (N= 423,399)	3.02 (2.68 to 3.4)	14.08 (12.83 to 15.45)		
Additional - Serotype 7F (N=394,423)	0.1 (0.08 to 0.12)	13.11 (11.99 to 14.33)		
Additional - Serotype 19A (N=399,423)	2.48 (2.27 to 2.7)	14.19 (13.11 to 15.35)		

Statistical analyses

Statistical analysis title	Statistical analysis for serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1

Statistical analysis title	Statistical analysis for serotype 6B

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.25

Statistical analysis title	Statistical analysis for serotype 9V

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.95

Statistical analysis title	Statistical analysis for Serotype 14

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.95

Statistical analysis title	Statistical analysis for Serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.42

Statistical analysis title	Statistical analysis for Serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	1.6

Statistical analysis title	Statistical analysis for Serotype 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.29

Statistical analysis title	statistical analysis for Additional serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	202.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	163.4
upper limit	251.18

Statistical analysis title	statistical analysis for Additional serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	9.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.67
upper limit	11.46

Statistical analysis title	statistical analysis for Additional serotype 5
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	12.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.86
upper limit	13.98

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	4.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.01
upper limit	5.41

Statistical analysis title	Statistical analysis for Additional serotype 7F
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	130.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	108.16
upper limit	157.58

Statistical analysis title	Statistical analysis for Additional serotype 19A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCsnwere significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	13vPnC Group 3 v 7vPnC Group 1
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	5.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.1
upper limit	6.44

Secondary: GMC for serotype-specific pneumococcal IgG antibody 1 month after the toddler dose, 13vPnC Group 4 vs 7vPnC Group 1

End point title	GMC for serotype-specific pneumococcal IgG antibody 1 month after the toddler dose, 13vPnC Group 4 vs 7vPnC Group 1[80]

End point description:

Antibody GMC for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes (Serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. GMC and corresponding 2-sided 95% CIs were evaluated. GMs were calculated using all subjects with available data for the specified blood draw. In the below table 'N' represents the number of subjects with a determinate antibody concentration for the specified serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[80] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	215		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=399, 215)	14.88 (11.34 to 14.03)	12.15 (10.8 to 13.67)		
7vPnC - Serotype 6B (N=399, 215)	11.94 (0.05 to 0.07)	11.92 (10.28 to 13.81)		
7vPnC - Serotype 9V (N= 399, 215)	8.36 (0.12 to 0.16)	7.23 (6.49 to 8.06)		
7vPnC - Serotype 14 (N=399, 215)	24.55 (0.61 to 0.67)	23.45 (21.08 to 26.09)		
7vPnC - Serotype 18C (N= 399, 215)	9.02 (2.68 to 3.4)	8.79 (7.73 to 9.99)		
7vPnC - Serotype 19F (N=399, 215)	11.36 (0.08 to 0.12)	22.13 (19.63 to 24.95)		
7vPnC - Serotype 23F (N=399, 215)	12.61 (2.27 to 2.7)	9.81 (8.4 to 11.45)		
Additional - Serotype 1 (N=347, 215)	0.06 (13.64 to 16.25)	12.55 (11.15 to 14.12)		
Additional - Serotype 3 (N= 370, 213)	0.14 (10.82 to 13.18)	1.63 (1.49 to 1.79)		
Additional - Serotype 5 (N=398, 215)	0.67 (7.7 to 9.08)	7.9 (7.15 to 8.72)		
Additional - Serotype 6A (N=399, 215)	3.02 (22.71 to 26.55)	14.18 (12.57 to 16.01)		
Additional - Serotype 7F (N=394, 215)	0.1 (8.29 to 9.82)	10.11 (9.06 to 11.28)		
Additional - Serotype 19A (N=399, 215)	2.48 (10.36 to 12.46)	16.71 (14.86 to 18.78)		

Statistical analyses

Statistical analysis title	Statistical analysis for serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.95

Statistical analysis title	Statistical analysis for serotype 6B

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.19

Statistical analysis title	Statistical analysis for serotype 9V

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.19

Statistical analysis title	Statistical analysis for serotype 14

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.99

Statistical analysis title	Statistical analysis for serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.12

Statistical analysis title	Statistical analysis for serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.39
upper limit	1.8

Statistical analysis title	Statistical analysis for serotype 23F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.13

Statistical analysis title	Statistical analysis for Additional serotype 1

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	200.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	160.75
upper limit	251.28

Statistical analysis title	Statistical analysis for Additional serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	12.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.58
upper limit	14.12

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	11.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.54
upper limit	13.62

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	3.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.19
upper limit	4.32

Statistical analysis title	Statistical analysis for Additional serotype 7F
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	96.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	80.28
upper limit	117.04

Statistical analysis title	Statistical analysis for Additional serotype 19A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. GMCs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMC ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	6.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.46
upper limit	6.97

Secondary: Percentage of Subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ after toddler dose, 13vPnC Group 2 vs 7vPnC Group 1

End point title	Percentage of Subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ after toddler dose, 13vPnC Group 2 vs 7vPnC Group 1[81]

End point description:

A randomly selected subset was analyzed for serum OPA elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1 and 2, blood samples (approximately 5 mL) were collected at the 6-, 12-, and 13-month visits. In the below table N = number of subjects with a determinate OPA antibody titer to the given serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[81] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	409		
Units: percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N= 113, 109)	100 (96.8 to 100)	100 (96.7 to 100)		
7vPnC - Serotype 6B (N=111, 109)	99.1 (95.1 to 100)	98.2 (93.5 to 99.8)		
7vPnC - Serotype 9V (N=113, 109)	100 (96.8 to 100)	100 (96.7 to 100)		
7vPnC - Serotype 14 (N=112, 109)	100 (96.8 to 100)	100 (96.7 to 100)		
7vPnC - Serotype 18C (N=111, 110)	100 (96.7 to 100)	100 (96.7 to 100)		
7vPnC - Serotype 19F (N=112,106)	97.3 (92.4 to 99.4)	98.1 (93.4 to 99.8)		
7vPnC - Serotype 23F (N= 112,108)	100 (96.8 to 100)	100 (96.6 to 100)		
Additional - Serotype 1 (N=113,108)	2.7 (0.6 to 7.6)	97.2 (92.1 to 99.4)		
Additional - Serotype 3 (N=113,110)	24.8 (17.1 to 33.8)	99.1 (95 to 100)		
Additional - Serotype 5 (N=113,111)	0.9 (0 to 4.8)	98.2 (93.6 to 99.8)		
Additional - Serotype 6A (N=111,108)	96.4 (91 to 99)	99.1 (94.9 to 100)		
Additional - Serotype 7F (N=92,108)	27.2 (18.4 to 37.4)	100 (96.6 to 100)		
Additional - Serotype 19A (N=106, 106)	67 (57.2 to 75.8)	99.1 (94.9 to 100)		

Statistical analyses

Statistical analysis title	Statistical analysis for serotype 4

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for serotype 6B

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	3.3

Statistical analysis title	Statistical analysis for serotype 9V

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for serotype 14

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for serotype 18C
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for serotype 19F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	5.9

Statistical analysis title	Statistical analysis for serotype 23F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for Additional serotype 3
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	74.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	65.2
upper limit	82.1

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	97.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	92.3
upper limit	99.4

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	8.1

Statistical analysis title	Statistical analysis for Additional serotype 7F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	72.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	62.6
upper limit	81.6

Statistical analysis title	Statistical analysis for Additional serotype 19A
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	32.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.1
upper limit	41.9

Secondary: Percentage of subjects achieving a pneumococcal OPA antibody titer ≥

LLOQ after toddler dose, 13vPnC Group 3 vs 7vPnC Group 1

End point title	Percentage of subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ after toddler dose, 13vPnC Group 3 vs 7vPnC Group 1[82]

End point description:

A randomly selected subset was analyzed for serum OPA elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Group 1, blood samples were collected at the 6-, 12-, and 13-month visits. For Group 3 subjects , blood samples were collected at the 7-, 12-, and 13 month visits. In the below table N = number of subjects with a determinate OPA antibody titer to the given serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[82] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	423		
Units: percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=113, 105)	100 (96.8 to 100)	100 (96.5 to 100)		
7vPnC - Serotype 6B (N=111, 103)	99.1 (95.1 to 100)	100 (96.5 to 100)		
7vPnC - Serotype 9V (N=113, 105)	100 (96.8 to 100)	100 (96.5 to 100)		
7vPnC - Serotype 14 (N=112, 106)	100 (96.7 to 100)	100 (96.6 to 100)		
7vPnC - Serotype 18C (N=111, 106)	100 (96.7 to 100)	100 (96.6 to 100)		
7vPnC - Serotype 19F (N=112,101)	97.3 (92.4 to 99.4)	100 (96.4 to 100)		
7vPnC - Serotype 23F (N=112, 103)	100 (96.8 to 100)	97.1 (91.7 to 99.4)		
Additional - Serotype 1 (N=113, 105)	2.7 (0.6 to 7.6)	99 (94.8 to 100)		
Additional - Serotype 3 (N=113, 107)	24.8 (17.1 to 33.8)	100 (96.6 to 100)		
Additional - Serotype 5 (N=113, 105)	0.9 (0 to 4.8)	99 (94.8 to 100)		
Additional - Serotype 6A (N=111,105)	96.4 (91 to 99)	100 (96.5 to 100)		
Additional - Serotype 7F (N= 92,104)	27.2 (18.4 to 37.4)	100 (96.5 to 100)		
Additional - Serotype 19A (N=106, 105)	67 (57.2 to 75.8)	100 (96.5 to 100)		

Statistical analyses

Statistical analysis title	Statistical analysis for Serotype 4

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other[83]
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	3.3

Notes:

[83] - CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed aspercentage.

Statistical analysis title	Statistical analysis for Serotype 6B

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other[84]
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	4.9

Notes:

[84] - CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed aspercentage.

Statistical analysis title	Statistical analysis for Serotype 9V

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other[85]
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	3.3

Notes:

[85] - CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed aspercentage.

Statistical analysis title	Statistical analysis for Serotype 14

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for Serotype 18C

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for serotype 19F

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	5.9

Statistical analysis title	Statistical analysis for serotype 23F
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for Additional serotype 1
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	94.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	88.3
upper limit	98

Statistical analysis title	Statistical analysis for Additional serotype 3
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	74.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	65.2
upper limit	82.1

Statistical analysis title	Statistical analysis for Additional serotype 5
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	97.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	92.3
upper limit	99.4

Statistical analysis title	Statistical analysis for Additional serotype 6A
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	8.1

Statistical analysis title	Statistical analysis for Additional serotype 7F

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	72.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	62.6
upper limit	81.6

Statistical analysis title	Statistical analysis for Additional serotype 19A

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	32.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.1
upper limit	41.9

Secondary: Percentage of subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ after toddler dose, 13vPnC Group 4 vs 7vPnC Group 1

End point title	Percentage of subjects achieving a pneumococcal OPA antibody titer ≥ LLOQ after toddler dose, 13vPnC Group 4 vs 7vPnC Group 1[86]

End point description:

A randomly selected subset was analyzed for serum OPA elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1, blood samples were collected at the 6-, 12-, and 13-month visits. For Group 4 subjects, blood samples were collected at the 6-, 12-, and 13 month visits. In the below table N = number of subjects with a determinate OPA antibody titer to the given serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[86] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	215		
Units: percentage of subjects				
number (confidence interval 95%)				
7vPnC - Serotype 4 (N=113, 108)	100 (96.8 to 100)	100 (96.6 to 100)		
7vPnC - Serotype 6B (N=111, 103)	99.1 (95.1 to 100)	96.1 (90.4 to 98.9)		
7vPnC - Serotype 9V (N= 113, 107)	100 (96.8 to 100)	99.1 (94.9 to 100)		
7vPnC - Serotype 14 (N=112, 107)	100 (96.8 to 100)	100 (96.6 to 100)		
7vPnC - Serotype 18C (N=111, 113)	100 (96.7 to 100)	100 (96.8 to 100)		
7vPnC - Serotype 19F (N=112, 106)	97.3 (92.4 to 99.4)	100 (96.6 to 100)		
7vPnC - Serotype 23F (N= 112, 104)	100 (96.8 to 100)	95.2 (89.1 to 98.4)		
Additional - Serotype 1 (N=113, 117)	2.7 (0.6 to 7.6)	98.3 (94 to 99.8)		
Additional - Serotype 3 (N=113,118)	24.8 (17.1 to 33.8)	99.2 (95.4 to 100)		
Additional - Serotype 5 (N=113,118)	0.9 (0 to 4.8)	99.2 (95.4 to 100)		
Additional - Serotype 6A (N=111,108)	96.4 (91 to 99)	100 (96.6 to 100)		
Additional - Serotype 7F (N=92,115)	27.2 (18.4 to 37.4)	99.1 (95.3 to 100)		
Additional - Serotype 19A (N=106,113)	67 (57.2 to 75.8)	99.1 (95.2 to 100)		

Statistical analyses

Statistical analysis title	Statistical analysis for Serotype 4

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for Serotype 4
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	1.6

Statistical analysis title	Statistical analysis for Serotype 9V
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	2.4

Statistical analysis title	Statistical analysis for Serotype 14
Statistical analysis description:	
CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.3

Statistical analysis title	Statistical analysis for Serotype 18C

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	3.3

Statistical analysis title	Statistical analysis for Serotype 19F

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	7.6

Statistical analysis title	Statistical analysis for Serotype 23F

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.9
upper limit	-1

Statistical analysis title	Statistical analysis for additional Serotype 1

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	95.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	90
upper limit	98.6

Statistical analysis title	Statistical analysis for additional Serotype 3

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	74.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	65.3
upper limit	82.1

Statistical analysis title	Statistical analysis for additional Serotype 5
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	98.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	93.9
upper limit	99.8

Statistical analysis title	Statistical analysis for additional Serotype 6B
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	3.3

Statistical analysis title	Statistical analysis for Additional serotype 7F
Statistical analysis description: CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.	
Comparison groups	13vPnC Group 4 v 7vPnC Group 1
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	72

Confidence interval	
level	95 %
sides	2-sided
lower limit	61.7
upper limit	80.7

Statistical analysis title	Statistical analysis for Additional serotype 19A

Statistical analysis description:

CI for the difference in proportions is computed using the Chan and Zhang procedure, 13vPnC-7vPnC reference, expressed as percentage.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	32.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.2
upper limit	41.9

Secondary: Serotype-specific OPA GMT 1 month after the toddler dose, 13vPnC Group 2 vs 7vPnC Group 1

End point title	Serotype-specific OPA GMT 1 month after the toddler dose, 13vPnC Group 2 vs 7vPnC Group 1[87]

End point description:

A randomly selected subset was analyzed for serum OPA GMT elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Groups 1 and 2, blood samples (approximately 5 mL) were collected at the 6-, 12-, and 13-month visits. In the below table 'N' represents the number of subjects with a determinate antibody titer for the specified serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[87] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	409		
Units: GMT				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=113, 109)	7662 (6171.2 to 9513.2)	6915 (5700.3 to 8389.1)		
7vPnC - Serotype 6B (N=111,109)	4958 (3931.7 to 6251.5)	4894 (3695.5 to 6481.9)		
7vPnC - Serotype 9V (N= 113,109)	7825 (6469.6 to 9463.4)	7679 (6251.4 to 9433.6)		
7vPnC - Serotype 14 (N=112, 109)	3269 (2773 to 3854.4)	2694 (2248.9 to 3226.7)		
7vPnC - Serotype 18C (N=111,110)	22011 (18687.5 to 25925.5)	20661 (16762.4 to 25467)		
7vPnC - Serotype 19F (N=112,106)	1410 (1066.7 to 1864.3)	3860 (2897.1 to 5144)		
7vPnC - Serotype 23F (N=112,108)	13098 (10963.1 to 15648.6)	11141 (8895.2 to 13953.7)		
Additional - Serotype 1 (N=113,108)	4 (3.9 to 4.8)	372 (299.8 to 460.7)		
Additional - Serotype 3 (N=113,110)	7 (5.8 to 8.8)	289 (246.8 to 338.5)		
Additional - Serotype 5 (N=113,111)	4 (3.9 to 4.8)	656 (527.7 to 816.5)		
Additional - Serotype 6A (N=111,108)	2569 (1879.1 to 3511.4)	10013 (7740.8 to 12952)		
Additional - Serotype 7F (N=92,108)	17 (10.5 to 28.8)	5141 (4373.1 to 6044.1)		
Additional - Serotype 19A (N=106,106)	48 (32.4 to 70.4)	1713 (1382.2 to 2124)		

Statistical analyses

Statistical analysis title	statistical analysis for serotype 4

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.21

Statistical analysis title	Statistical analysis for serotype 6B
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.42

Statistical analysis title	Statistical analysis for serotype 9V
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.3

Statistical analysis title	Statistical analysis for serotype 14
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2

Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.05

Statistical analysis title	Statistical analysis for serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.22

Statistical analysis title	Statistical analysis for serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.84
upper limit	4.08

Statistical analysis title	Statistical analysis for serotype 23F
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.13

Statistical analysis title	Statistical analysis for Additional serotype 1
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	85.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	68.25
upper limit	108.01

Statistical analysis title	Statistical analysis for Additional serotype 3
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	40.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	31.26
upper limit	52.74

Statistical analysis title	Statistical analysis for Additional serotype 5

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	160.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	128.62
upper limit	199.75

Statistical analysis title	Statistical analysis for Additional serotype 6A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratio.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	5.84

Statistical analysis title	Statistical analysis for Additional serotype 7F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	296.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	180.45
upper limit	485.91

Statistical analysis title	Statistical analysis for Additional serotype 19A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 2 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 2
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	35.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.09
upper limit	55.68

Secondary: Serotype-specific OPA GMT 1 month after the toddler dose, 13vPnC Group 3 vs 7vPnC Group 1

End point title	Serotype-specific OPA GMT 1 month after the toddler dose, 13vPnC Group 3 vs 7vPnC Group 1[88]

End point description:

A randomly selected subset was analyzed for serum OPA GMT elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Group 1, blood samples were collected at the 6-, 12-, and 13- month visits. For Group 3 subjects, blood samples were collected at the 7-, 12-, and 13 month visits. In the below table 'N' represents the number of subjects with a determinate antibody titer for the specified serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[88] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	423		
Units: GMT				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N= 113, 105)	7662 (32.4 to 70.4)	7319 (5960.5 to 8988)		
7vPnC - Serotype 6B (N= 111,103)	4958 (6171.2 to 9513.2)	5740 (4723.9 to 6975.2)		
7vPnC - Serotype 9V (N=113,105)	7825 (3931.7 to 6251.5)	8892 (7563.3 to 10452.9)		
7vPnC - Serotype 14 (N= 112,106)	3269 (6469.6 to 9463.4)	2776 (2268.6 to 3396.8)		
7vPnC - Serotype 18C (N= 111, 106)	22011 (2773 to 3854.4)	20098 (17265.9 to 23393.5)		
7vPnC - Serotype 19F (N=112, 101)	1410 (18687.5 to 25925.5)	4513 (3685.1 to 5528.1)		
7vPnC - Serotype 23F (N=112, 103)	13098 (1066.7 to 1864.3)	9845 (7137.2 to 13578.9)		
Additional - Serotype 1 (N=113, 105)	4 (10963.1 to 15648.6)	424 (349 to 516.1)		
Additional - Serotype 3 (N=113, 107)	7 (3.9 to 4.8)	309 (269 to 354.8)		
Additional - Serotype 5 (N=113, 105)	4 (5.8 to 8.8)	727 (592.6 to 891.6)		
Additional - Serotype 6A (N= 111,105)	2569 (3.9 to 4.3)	11347 (9501.1 to 13551.5)		
Additional - Serotype 7F (N=92,104)	17 (1879.1 to 3511.4)	7123 (6163.8 to 8230.9)		
Additional - Serotype 19A (N=106,105)	48 (10.5 to 28.8)	2041 (1753.6 to 2376.4)		

Statistical analyses

Statistical analysis title	Statistical analysis for serotype 4
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.29

Statistical analysis title	Statistical analysis for serotype 6B
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.57

Statistical analysis title	Statistical analysis for Serotype 9V
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.46

Statistical analysis title	Statistical analysis for Serotype 18C
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3

Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.14

Statistical analysis title	Statistical analysis for Serotype 14

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.1

Statistical analysis title	Statistical analysis for Serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.26
upper limit	4.45

Statistical analysis title	Statistical analysis for Serotype 23F
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.07

Statistical analysis title	Statistical analysis for additional Serotype 1
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	98.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	79.41
upper limit	121.08

Statistical analysis title	Statistical analysis for additional Serotype 5
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	177.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	145.12
upper limit	217.11

Statistical analysis title	Statistical analysis for additional Serotype 3

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	43.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	33.73
upper limit	55.85

Statistical analysis title	Statistical analysis for additional Serotype 6A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.07
upper limit	6.35

Statistical analysis title	Statistical analysis for additional Serotype 7F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	410.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	249.67
upper limit	674.1

Statistical analysis title	Statistical analysis for additional Serotype 19A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPA GMTs were significantly higher in 13vPnC Group 3 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 3
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT ratio
Point estimate	42.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.22
upper limit	64.69

Secondary: Serotype-specific OPA GMT 1 month after the toddler dose, 13vPnC Group 4 vs 7vPnC Group 1

End point title	Serotype-specific OPA GMT 1 month after the toddler dose, 13vPnC Group 4 vs 7vPnC Group 1[89]

End point description:

A randomly selected subset was analyzed for serum OPA GMT elicited by the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). For subjects in Group1 1, blood samples were collected at the 6-, 12-, and 13- month visits. For Group 4 subjects, blood samples were collected at the 6-, 12-, and 13 month visits. In the below table 'N' represents the number of subjects with a determinate antibody titer for the specified serotype. Evaluable toddler pneumococcal immunogenicity population included subjects aged 41 to 78 days, received vaccinations as they were randomized to receive, had valid and determinate pneumococcal assay result, had blood draw after toddler dose within the required time frame, received no prohibited vaccines and had no major protocol deviation.

End point type	Secondary

End point timeframe:

1 month after the toddler dose (13 Months of age)

Notes:

[89] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period.

End point values	7vPnC Group 1	13vPnC Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	399	215		
Units: GMT				
geometric mean (confidence interval 95%)				
7vPnC - Serotype 4 (N=113, 108)	7662 (3931.7 to 6251.5)	7193 (5716.6 to 9049.6)		
7vPnC - Serotype 6B (N=111,103)	4958 (6469.6 to 9463.4)	2713 (1973.3 to 3729.5)		
7vPnC - Serotype 9V (N=113, 107)	7825 (2773 to 3854.4)	7861 (6237.6 to 9907.1)		
7vPnC - Serotype 14 (N=112, 107)	3269 (18687.5 to 25925.5)	2928 (2481.8 to 3453.7)		
7vPnC - Serotype 18C (N=111, 113)	22011 (6171.2 to 9513.2)	18425 (15495.1 to 21909)		
7vPnC - Serotype 19F (N=112, 106)	1410 (1066.7 to 1864.3)	3636 (3046.5 to 4340)		
7vPnC - Serotype 23F (N=112, 104)	13098 (10963.1 to 15648.6)	6255 (4289.5 to 9120.3)		
Additional - Serotype 1 (N=113,117)	4 (3.9 to 4.8)	391 (317.7 to 480.4)		
Additional - Serotype 3 (N=113,118)	7 (5.8 to 8.8)	351 (305.5 to 402.9)		
Additional - Serotype 5 (N=113,118)	4 (3.9 to 4.3)	661 (547.7 to 797.8)		
Additional - Serotype 6A (N=111,108)	2569 (1879.1 to 3511.4)	7755 (6548.9 to 9184)		
Additional - Serotype 7F (N=92,115)	17 (10.5 to 28.8)	5700 (4741.5 to 6853.3)		
Additional - Serotype 19A (N=106,113)	48 (32.4 to 70.4)	1503 (1209.3 to 1868.5)		

Statistical analyses

Statistical analysis title	Statistical analysis for serotype 4
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.28

Statistical analysis title	Statistical analysis for serotype 6B
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.81

Statistical analysis title	Statistical analysis for serotype 9V
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.13

Statistical analysis title	Statistical analysis for serotype 14
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4

Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.13

Statistical analysis title	Statistical analysis for serotype 18C

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	11.06

Statistical analysis title	Statistical analysis for serotype 19F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.85
upper limit	3.6

Statistical analysis title	Statistical analysis for serotype 23F
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.72

Statistical analysis title	Statistical analysis for additional serotype 1
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	90.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	71.82
upper limit	113.42

Statistical analysis title	Statistical analysis for additional serotype 3
Statistical analysis description:	
CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.	
Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	49.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	38.49
upper limit	63.12

Statistical analysis title	Statistical analysis for additional serotype 5

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	161.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	132.63
upper limit	196.46

Statistical analysis title	Statistical analysis for additional serotype 6A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.11
upper limit	4.31

Statistical analysis title	Statistical analysis for additional serotype 7F

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	328.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	200.4
upper limit	537.89

Statistical analysis title	Statistical analysis for additional serotype 19A

Statistical analysis description:

CIs of ratio are back transformations of CI based on Student t distribution for mean difference of logarithms of measures. OPAGMTs were significantly higher in 13vPnC Group 4 than 7vPnC Group 1 if lower bound of 95% CI GMT ratios >1.

Comparison groups	7vPnC Group 1 v 13vPnC Group 4
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMT ratio
Point estimate	31.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.37
upper limit	48.58

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs/ SAEs: recorded from informed consent till the end of study (up to 18 months of age).Subjects recorded prespecified AEs in electronic diary:local reactions; systemic events; (within 7 days post 13vPnC or 7vPnc dose for infant and toddler doses).

Adverse event reporting additional description:

Adverse events(AEs) and Serious AEs were grouped by system organ class and summarized. AEs included solicited/unsolicited AEs collected in electronic diary (local and systemic reactions;systematic assessment) collected on case report form at each visit (nonsystematic assessment).LRs/SEs were assessed for infant and toddler dose groups.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	7vPnC Group 1

Reporting group description:

Subjects received 7vPnC vaccine administered at 3, 4, 5, and 12 months of age. Single dose (0.5 mL) of 7vPnC was administered intramuscularly into the anterolateral muscle of the left thigh.

Reporting group title	13vPnC Group 2

Reporting group description:

Subjects received 13vPnC vaccine administered at 3, 4, 5, and 12 months of age. Single dose (0.5 mL) of 13vPnCwas administered intramuscularly into the anterolateral muscle of the left thigh.

Reporting group title	13vPnC Group 3

Reporting group description:

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

Reporting group title	13vPnC Group 4

Reporting group description:

Subjects received 13vPnC vaccine administered at 3, 5, and 12 months of age. Single dose (0.5 mL) of 13vPnC was administered intramuscularly into the anterolateral muscle of the left thigh.

Serious adverse events	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 472 (1.27%)	10 / 472 (2.12%)	11 / 474 (2.32%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphangioma			
subjects affected / exposed[1]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (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
Congenital, familial and genetic disorders			

Cerebral palsy			
subjects affected / exposed[2]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (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
Heart disease congenital			
subjects affected / exposed[3]	0 / 472 (0.00%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular septal defect			
subjects affected / exposed[4]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (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
Nervous system disorders			
Coordination abnormal			
subjects affected / exposed[5]	0 / 472 (0.00%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed[6]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (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
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed[7]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (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
Inguinal hernia			
subjects affected / exposed[8]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (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			
Bronchiolitis			

subjects affected / exposed[9]	0 / 472 (0.00%)	1 / 471 (0.21%)	3 / 474 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed[10]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (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
Bronchopneumonia			
subjects affected / exposed[11]	3 / 472 (0.64%)	7 / 471 (1.49%)	4 / 474 (0.84%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			
subjects affected / exposed[12]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (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
Measles			
subjects affected / exposed[13]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (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
Oral candidiasis			
subjects affected / exposed[14]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (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
Pharyngitis			
subjects affected / exposed[15]	0 / 472 (0.00%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed[16]	1 / 472 (0.21%)	1 / 471 (0.21%)	1 / 474 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed[17]	0 / 472 (0.00%)	1 / 471 (0.21%)	2 / 474 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	13vPnC Group 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 234 (2.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphangioma			
subjects affected / exposed[1]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Cerebral palsy			
subjects affected / exposed[2]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Heart disease congenital			
subjects affected / exposed[3]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular septal defect			
subjects affected / exposed[4]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Coordination abnormal			
subjects affected / exposed[5]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Partial seizures			

subjects affected / exposed[6]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed[7]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed[8]	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed[9]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed[10]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed[11]	4 / 234 (1.71%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Hand-foot-and-mouth disease			
subjects affected / exposed[12]	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Measles			
subjects affected / exposed[13]	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			

subjects affected / exposed[14]	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed[15]	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed[16]	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed[17]	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

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

Non-serious adverse events	7vPnC Group 1	13vPnC Group 2	13vPnC Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	159 / 472 (33.69%)	166 / 472 (35.17%)	130 / 474 (27.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed[18]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Heart disease congenital			
subjects affected / exposed[19]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Hypersomnia			
subjects affected / exposed[20]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed[21]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Crying			
subjects affected / exposed[22]	1 / 472 (0.21%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	1	1	0

Injection site erythema			
subjects affected / exposed[23]	12 / 472 (2.54%)	13 / 471 (2.76%)	10 / 474 (2.11%)
occurrences (all)	13	14	10
Injection site swelling			
subjects affected / exposed[24]	2 / 472 (0.42%)	2 / 471 (0.42%)	0 / 474 (0.00%)
occurrences (all)	2	2	0
Pyrexia			
subjects affected / exposed[25]	5 / 472 (1.06%)	5 / 471 (1.06%)	11 / 474 (2.32%)
occurrences (all)	6	6	11
Temperature ≥38°C: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[26]	3 / 470 (0.64%)	5 / 472 (1.06%)	8 / 472 (1.69%)
occurrences (all)	3	5	8
Temperature ≥38°C but ≤39°C : Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[27]	3 / 470 (0.64%)	5 / 472 (1.06%)	8 / 472 (1.69%)
occurrences (all)	3	5	8
Decreased Appetite:Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[28]	20 / 470 (4.26%)	9 / 472 (1.91%)	22 / 471 (4.67%)
occurrences (all)	20	9	22
Irritability: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[29]	22 / 470 (4.68%)	16 / 472 (3.39%)	58 / 472 (12.29%)
occurrences (all)	22	16	58
Increased sleep: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			

alternative assessment type: Systematic			
subjects affected / exposed[30]	12 / 470 (2.55%)	3 / 472 (0.64%)	35 / 471 (7.43%)
occurrences (all)	12	3	35
Decreased Sleep: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[31]	13 / 470 (2.77%)	9 / 472 (1.91%)	27 / 471 (5.73%)
occurrences (all)	13	9	27
Temperature ≥ 38°C : Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[32]	4 / 459 (0.87%)	7 / 462 (1.52%)	8 / 459 (1.74%)
occurrences (all)	4	7	8
Decreased appetite: Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[33]	12 / 459 (2.61%)	9 / 462 (1.95%)	9 / 459 (1.96%)
occurrences (all)	12	9	9
Irritability: Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[34]	25 / 459 (5.45%)	17 / 462 (3.68%)	15 / 460 (3.26%)
occurrences (all)	25	17	15
Increased sleep: Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[35]	3 / 459 (0.65%)	0 / 462 (0.00%)	1 / 459 (0.22%)
occurrences (all)	3	0	1
Decreased sleep: Infant series Dose	Additional description: Subjects affected and		

2	occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[36] occurrences (all)	8 / 459 (1.74%) 8	8 / 462 (1.73%) 8	6 / 459 (1.31%) 6
Temperature ≥ 38°C : Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[37] occurrences (all)	8 / 463 (1.73%) 8	10 / 467 (2.14%) 10	8 / 460 (1.74%) 8
Temperature ≥38°C but ≤39°C : Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[38] occurrences (all)	7 / 463 (1.51%) 7	9 / 467 (1.93%) 9	8 / 460 (1.74%) 8
Temperature >39°C but ≤40°C: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[39] occurrences (all)	1 / 463 (0.22%) 1	1 / 467 (0.21%) 1	1 / 460 (0.22%) 1
Decreased appetite: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[40] occurrences (all)	11 / 463 (2.38%) 11	6 / 467 (1.28%) 6	11 / 460 (2.39%) 11
Irritability: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic			

subjects affected / exposed	11 / 472 (2.33%)	10 / 472 (2.12%)	20 / 474 (4.22%)
occurrences (all)	11	10	20
Increased sleep: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[41]	3 / 463 (0.65%)	2 / 467 (0.43%)	2 / 460 (0.43%)
occurrences (all)	3	2	2
Decreased sleep: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[42]	1 / 463 (0.22%)	4 / 467 (0.86%)	6 / 460 (1.30%)
occurrences (all)	1	4	6
Temperature ≥ 38°C : after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[43]	14 / 432 (3.24%)	30 / 447 (6.71%)	30 / 446 (6.73%)
occurrences (all)	14	30	30
Temperature ≥38°C but ≤39°C : after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[44]	14 / 432 (3.24%)	29 / 447 (6.49%)	28 / 446 (6.28%)
occurrences (all)	14	29	28
Temperature >39°C but ≤40°C: after toddler dose			
subjects affected / exposed	1 / 472 (0.21%)	4 / 472 (0.85%)	2 / 474 (0.42%)
occurrences (all)	1	4	2
Decreased appetite: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			

subjects affected / exposed[45]	15 / 433 (3.46%)	11 / 447 (2.46%)	11 / 446 (2.47%)
occurrences (all)	15	11	11
Irritability: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic			
subjects affected / exposed[46]	19 / 432 (4.40%)	15 / 447 (3.36%)	16 / 446 (3.59%)
occurrences (all)	19	15	16
Increased sleep: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic			
subjects affected / exposed[47]	3 / 432 (0.69%)	0 / 447 (0.00%)	0 / 446 (0.00%)
occurrences (all)	3	0	0
Decreased sleep: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic			
subjects affected / exposed[48]	7 / 432 (1.62%)	10 / 447 (2.24%)	7 / 446 (1.57%)
occurrences (all)	7	10	7
Temperature ≥38°C but ≤39°C: Infant series dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic			
subjects affected / exposed[49]	4 / 459 (0.87%)	7 / 462 (1.52%)	8 / 459 (1.74%)
occurrences (all)	4	7	8
Eye disorders			
Dacryoadenitis acquired			
subjects affected / exposed[50]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[51]	21 / 472 (4.45%)	24 / 471 (5.10%)	15 / 474 (3.16%)
occurrences (all)	22	24	16
Dyspepsia			

subjects affected / exposed[52]	9 / 472 (1.91%)	12 / 471 (2.55%)	5 / 474 (1.05%)
occurrences (all)	9	12	5
Mouth ulceration			
subjects affected / exposed[53]	0 / 472 (0.00%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences (all)	0	0	1
Enteritis			
subjects affected / exposed[54]	12 / 472 (2.54%)	13 / 471 (2.76%)	5 / 474 (1.05%)
occurrences (all)	13	13	5
Vomiting			
subjects affected / exposed[55]	0 / 472 (0.00%)	1 / 471 (0.21%)	1 / 474 (0.21%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Alveolitis allergic			
subjects affected / exposed[56]	0 / 472 (0.00%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed[57]	0 / 472 (0.00%)	1 / 471 (0.21%)	1 / 474 (0.21%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed[58]	5 / 472 (1.06%)	4 / 471 (0.85%)	4 / 474 (0.84%)
occurrences (all)	5	4	4
Rhinorrhoea			
subjects affected / exposed[59]	1 / 472 (0.21%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences (all)	1	0	1
Wheezing			
subjects affected / exposed[60]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed[61]	2 / 472 (0.42%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences (all)	2	0	1
Rash			
subjects affected / exposed[62]	1 / 472 (0.21%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	1	1	0
Erythema			

subjects affected / exposed[63]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed[64]	0 / 472 (0.00%)	1 / 471 (0.21%)	1 / 474 (0.21%)
occurrences (all)	0	1	1
Redness (any): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[65]	19 / 470 (4.04%)	15 / 472 (3.18%)	27 / 472 (5.72%)
occurrences (all)	19	15	27
Redness (Mild): Infant Series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[66]	19 / 470 (4.04%)	15 / 472 (3.18%)	26 / 472 (5.51%)
occurrences (all)	19	15	26
Redness (Moderate): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[67]	1 / 470 (0.21%)	0 / 472 (0.00%)	3 / 471 (0.64%)
occurrences (all)	1	0	3
Swelling (Any): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[68]	26 / 470 (5.53%)	19 / 472 (4.03%)	26 / 472 (5.51%)
occurrences (all)	26	19	26
Swelling (mild): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[69]	23 / 470 (4.89%)	16 / 472 (3.39%)	24 / 472 (5.08%)
occurrences (all)	23	16	24
Swelling (Moderate): Infant series	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one		

Dose 1	occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[70] occurrences (all)	5 / 470 (1.06%) 5	3 / 472 (0.64%) 3	5 / 471 (1.06%) 5
Tenderness (any): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[71] occurrences (all)	20 / 470 (4.26%) 20	15 / 472 (3.18%) 15	36 / 472 (7.63%) 36
Tenderness (Present): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[72] occurrences (all)	18 / 470 (3.83%) 18	14 / 472 (2.97%) 14	36 / 472 (7.63%) 36
Tenderness (Significant): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[73] occurrences (all)	2 / 470 (0.43%) 2	1 / 472 (0.21%) 1	0 / 472 (0.00%) 0
Redness (any): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 subjects affected / exposed[74] occurrences (all)	13 / 459 (2.83%) 13	10 / 462 (2.16%) 10	20 / 460 (4.35%) 20
Redness (Moderate): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[75] occurrences (all)	2 / 459 (0.44%) 2	3 / 462 (0.65%) 3	3 / 460 (0.65%) 3
Redness (Mild): Infant Series Dose 2	Additional description: Additional description: Subjects affected and occurrences		

	for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[76]	12 / 459 (2.61%)	8 / 462 (1.73%)	18 / 460 (3.91%)
occurrences (all)	12	8	18
Swelling (Any): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[77]	16 / 459 (3.49%)	11 / 462 (2.38%)	19 / 459 (4.14%)
occurrences (all)	16	11	19
Swelling (mild): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[78]	15 / 459 (3.27%)	10 / 462 (2.16%)	17 / 459 (3.70%)
occurrences (all)	15	10	17
Swelling (Moderate): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[79]	3 / 459 (0.65%)	2 / 462 (0.43%)	2 / 459 (0.44%)
occurrences (all)	3	2	2
Tenderness (any): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[80]	13 / 459 (2.83%)	11 / 462 (2.38%)	28 / 460 (6.09%)
occurrences (all)	13	11	28
Tenderness (Present): Infant series Dose 2	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[81]	12 / 459 (2.61%)	9 / 462 (1.95%)	28 / 459 (6.10%)
occurrences (all)	12	9	28
Tenderness (Significant): Infant	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-		

series Dose 2	diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[82] occurrences (all)	1 / 459 (0.22%) 1	2 / 462 (0.43%) 2	0 / 460 (0.00%) 0
Redness (any): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[83] occurrences (all)	9 / 463 (1.94%) 9	10 / 467 (2.14%) 10	8 / 460 (1.74%) 8
Redness (Mild): Infant Series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[84] occurrences (all)	8 / 463 (1.73%) 8	10 / 467 (2.14%) 10	5 / 460 (1.09%) 5
Redness (Moderate): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRsand SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[85] occurrences (all)	1 / 463 (0.22%) 1	1 / 467 (0.21%) 1	4 / 460 (0.87%) 4
Swelling (Any): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[86] occurrences (all)	9 / 463 (1.94%) 9	9 / 467 (1.93%) 9	11 / 460 (2.39%) 11
Swelling (mild): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic			

subjects affected / exposed[87]	9 / 463 (1.94%)	9 / 467 (1.93%)	10 / 460 (2.17%)
occurrences (all)	9	9	10
Swelling (Moderate): Infant series Dose 3	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[88]	0 / 463 (0.00%)	1 / 467 (0.21%)	3 / 460 (0.65%)
occurrences (all)	0	1	3
Tenderness (any): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[89]	23 / 463 (4.97%)	16 / 467 (3.43%)	16 / 460 (3.48%)
occurrences (all)	23	16	16
Tenderness (Present): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[90]	20 / 463 (4.32%)	15 / 467 (3.21%)	15 / 460 (3.26%)
occurrences (all)	20	15	15
Tenderness (Significant): Infant series Dose 3	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[91]	3 / 463 (0.65%)	1 / 467 (0.21%)	1 / 460 (0.22%)
occurrences (all)	3	1	1
Redness (any): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[92]	9 / 432 (2.08%)	15 / 447 (3.36%)	16 / 446 (3.59%)
occurrences (all)	9	15	16
Redness (Mild): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[93]	6 / 432 (1.39%)	11 / 447 (2.46%)	11 / 446 (2.47%)
occurrences (all)	6	11	11
Redness (Moderate): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			

subjects affected / exposed[94]	6 / 432 (1.39%)	7 / 447 (1.57%)	6 / 446 (1.35%)
occurrences (all)	6	7	6
Swelling (Any): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
subjects affected / exposed[95]	15 / 432 (3.47%)	16 / 447 (3.58%)	16 / 446 (3.59%)
occurrences (all)	15	16	16
Swelling (mild):After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[96]	10 / 432 (2.31%)	12 / 447 (2.68%)	12 / 446 (2.69%)
occurrences (all)	10	12	12
Swelling (Moderate): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[97]	7 / 432 (1.62%)	6 / 447 (1.34%)	6 / 446 (1.35%)
occurrences (all)	7	6	6
Swelling (Severe): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[98]	0 / 432 (0.00%)	0 / 447 (0.00%)	0 / 446 (0.00%)
occurrences (all)	0	0	0
Tenderness (any): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[99]	28 / 432 (6.48%)	22 / 447 (4.92%)	24 / 446 (5.38%)
occurrences (all)	28	22	24
Tenderness (Present): After toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[100]	28 / 432 (6.48%)	20 / 447 (4.47%)	21 / 446 (4.71%)
occurrences (all)	28	20	21
Tenderness (Significant): After toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[101]	0 / 432 (0.00%)	2 / 447 (0.45%)	3 / 446 (0.67%)
occurrences (all)	0	2	3

Redness (Severe): After toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[102]	0 / 432 (0.00%)	0 / 447 (0.00%)	0 / 446 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed[103]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed[104]	10 / 472 (2.12%)	11 / 471 (2.34%)	6 / 474 (1.27%)
occurrences (all)	10	11	6
Bronchopneumonia			
subjects affected / exposed[105]	7 / 472 (1.48%)	7 / 471 (1.49%)	7 / 474 (1.48%)
occurrences (all)	7	7	7
Gastroenteritis			
subjects affected / exposed[106]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed[107]	0 / 472 (0.00%)	0 / 471 (0.00%)	1 / 474 (0.21%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed[108]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed[109]	97 / 472 (20.55%)	91 / 471 (19.32%)	68 / 474 (14.35%)
occurrences (all)	122	123	91
Oral candidiasis			
subjects affected / exposed[110]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed[111]	1 / 472 (0.21%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	1	0	0
Pneumonia			

subjects affected / exposed[112]	1 / 472 (0.21%)	3 / 471 (0.64%)	2 / 474 (0.42%)
occurrences (all)	1	3	2
Rhinitis			
subjects affected / exposed[113]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed[114]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed[115]	38 / 472 (8.05%)	34 / 471 (7.22%)	31 / 474 (6.54%)
occurrences (all)	43	38	35
Tracheitis			
subjects affected / exposed[116]	2 / 472 (0.42%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	2	1	0
Viral skin infection			
subjects affected / exposed[117]	0 / 472 (0.00%)	0 / 471 (0.00%)	0 / 474 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Calcium deficiency			
subjects affected / exposed[118]	0 / 472 (0.00%)	1 / 471 (0.21%)	0 / 474 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	13vPnC Group 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 234 (31.20%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed[18]	0 / 234 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Heart disease congenital			
subjects affected / exposed[19]	1 / 234 (0.43%)		
occurrences (all)	1		
Nervous system disorders			
Hypersomnia			

subjects affected / exposed[20]	0 / 234 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed[21]	0 / 234 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Crying			
subjects affected / exposed[22]	0 / 234 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed[23]	6 / 234 (2.56%)		
occurrences (all)	6		
Injection site swelling			
subjects affected / exposed[24]	1 / 234 (0.43%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed[25]	3 / 234 (1.28%)		
occurrences (all)	3		
Temperature ≥38°C: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[26]	3 / 233 (1.29%)		
occurrences (all)	3		
Temperature ≥38°C but ≤39°C : Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[27]	3 / 233 (1.29%)		
occurrences (all)	3		
Decreased Appetite:Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			

subjects affected / exposed[28]	4 / 233 (1.72%)		
occurrences (all)	4		
Irritability: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[29]	10 / 233 (4.29%)		
occurrences (all)	10		
Increased sleep: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[30]	2 / 233 (0.86%)		
occurrences (all)	2		
Decreased Sleep: Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[31]	6 / 233 (2.58%)		
occurrences (all)	6		
Temperature ≥ 38°C : Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[32]	3 / 232 (1.29%)		
occurrences (all)	3		
Decreased appetite: Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[33]	1 / 232 (0.43%)		
occurrences (all)	1		
Irritability: Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		

alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[34] occurrences (all)	2 / 232 (0.86%) 2		
Increased sleep: Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[35] occurrences (all)	1 / 232 (0.43%) 1		
Decreased sleep: Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[36] occurrences (all)	0 / 232 (0.00%) 0		
Temperature ≥ 38°C : Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[37] occurrences (all)	0 / 234 (0.00%) 0		
Temperature ≥38°C but ≤39°C : Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[38] occurrences (all)	0 / 234 (0.00%) 0		
Temperature >39°C but ≤40°C: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic			

subjects affected / exposed[39]	0 / 234 (0.00%)		
occurrences (all)	0		
Decreased appetite: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[40]	0 / 234 (0.00%)		
occurrences (all)	0		
Irritability: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences (all)	0		
Increased sleep: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[41]	0 / 234 (0.00%)		
occurrences (all)	0		
Decreased sleep: Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[42]	0 / 234 (0.00%)		
occurrences (all)	0		
Temperature ≥ 38°C : after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[43]	14 / 225 (6.22%)		
occurrences (all)	14		
Temperature ≥38°C but ≤39°C : after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		

alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[44]	14 / 225 (6.22%)		
occurrences (all)	14		
Temperature >39°C but ≤40°C: after toddler dose			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences (all)	0		
Decreased appetite: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[45]	5 / 225 (2.22%)		
occurrences (all)	5		
Irritability: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[46]	7 / 225 (3.11%)		
occurrences (all)	7		
Increased sleep: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[47]	1 / 225 (0.44%)		
occurrences (all)	1		
Decreased sleep: after toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[48]	2 / 225 (0.89%)		
occurrences (all)	2		
Temperature ≥38°C but ≤39°C: Infant series dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		

alternative dictionary used: Systemic events 0.0 alternative assessment type: Systematic subjects affected / exposed[49] occurrences (all)	3 / 232 (1.29%) 3		
Eye disorders Dacryoadenitis acquired subjects affected / exposed[50] occurrences (all)	1 / 234 (0.43%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed[51] occurrences (all) Dyspepsia subjects affected / exposed[52] occurrences (all) Mouth ulceration subjects affected / exposed[53] occurrences (all) Enteritis subjects affected / exposed[54] occurrences (all) Vomiting subjects affected / exposed[55] occurrences (all)	12 / 234 (5.13%) 14 3 / 234 (1.28%) 3 0 / 234 (0.00%) 0 4 / 234 (1.71%) 4 0 / 234 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Alveolitis allergic subjects affected / exposed[56] occurrences (all) Nasal congestion subjects affected / exposed[57] occurrences (all) Cough subjects affected / exposed[58] occurrences (all) Rhinorrhoea	0 / 234 (0.00%) 0 0 / 234 (0.00%) 0 2 / 234 (0.85%) 2		

subjects affected / exposed[59]	0 / 234 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed[60]	1 / 234 (0.43%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed[61]	0 / 234 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed[62]	0 / 234 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed[63]	0 / 234 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed[64]	0 / 234 (0.00%)		
occurrences (all)	0		
Redness (any): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[65]	8 / 233 (3.43%)		
occurrences (all)	8		
Redness (Mild): Infant Series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[66]	8 / 233 (3.43%)		
occurrences (all)	8		
Redness (Moderate): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[67]	0 / 233 (0.00%)		
occurrences (all)	0		

Swelling (Any): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[68]	13 / 233 (5.58%)		
occurrences (all)	13		
Swelling (mild): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[69]	12 / 233 (5.15%)		
occurrences (all)	12		
Swelling (Moderate): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[70]	2 / 233 (0.86%)		
occurrences (all)	2		
Tenderness (any): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[71]	12 / 233 (5.15%)		
occurrences (all)	12		
Tenderness (Present): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[72]	9 / 233 (3.86%)		
occurrences (all)	9		
Tenderness (Significant): Infant series Dose 1	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			

subjects affected / exposed[73]	3 / 233 (1.29%)		
occurrences (all)	3		
Redness (any): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
subjects affected / exposed[74]	4 / 232 (1.72%)		
occurrences (all)	4		
Redness (Moderate): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[75]	0 / 232 (0.00%)		
occurrences (all)	0		
Redness (Mild): Infant Series Dose 2	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[76]	4 / 232 (1.72%)		
occurrences (all)	4		
Swelling (Any): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[77]	4 / 232 (1.72%)		
occurrences (all)	4		
Swelling (mild): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[78]	4 / 232 (1.72%)		
occurrences (all)	4		
Swelling (Moderate): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			

subjects affected / exposed[79]	1 / 232 (0.43%)		
occurrences (all)	1		
Tenderness (any): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[80]	6 / 232 (2.59%)		
occurrences (all)	6		
Tenderness (Present): Infant series Dose 2	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[81]	6 / 232 (2.59%)		
occurrences (all)	6		
Tenderness (Significant): Infant series Dose 2	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[82]	0 / 232 (0.00%)		
occurrences (all)	0		
Redness (any): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[83]	0 / 234 (0.00%)		
occurrences (all)	0		
Redness (Mild): Infant Series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[84]	0 / 234 (0.00%)		
occurrences (all)	0		
Redness (Moderate): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRsand SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			

alternative assessment type: Systematic			
subjects affected / exposed[85]	0 / 234 (0.00%)		
occurrences (all)	0		
Swelling (Any): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[86]	0 / 234 (0.00%)		
occurrences (all)	0		
Swelling (mild): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[87]	0 / 234 (0.00%)		
occurrences (all)	0		
Swelling (Moderate): Infant series Dose 3	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e -diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			
subjects affected / exposed[88]	0 / 234 (0.00%)		
occurrences (all)	0		
Tenderness (any): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[89]	0 / 234 (0.00%)		
occurrences (all)	0		
Tenderness (Present): Infant series Dose 3	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[90]	0 / 234 (0.00%)		
occurrences (all)	0		
Tenderness (Significant): Infant series Dose 3	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic			

subjects affected / exposed[91] occurrences (all)	0 / 234 (0.00%) 0		
Redness (any): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[92] occurrences (all)	4 / 225 (1.78%) 4		
Redness (Mild): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[93] occurrences (all)	1 / 225 (0.44%) 1		
Redness (Moderate): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[94] occurrences (all)	3 / 225 (1.33%) 3		
Swelling (Any): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
subjects affected / exposed[95] occurrences (all)	7 / 225 (3.11%) 7		
Swelling (mild):After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[96] occurrences (all)	4 / 225 (1.78%) 4		
Swelling (Moderate): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[97] occurrences (all)	4 / 225 (1.78%) 4		
Swelling (Severe): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[98] occurrences (all)	1 / 225 (0.44%) 1		
Tenderness (any): After toddler dose	Additional description: Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to		

	distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[99] occurrences (all)	12 / 225 (5.33%) 12		
Tenderness (Present): After toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e--diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[100] occurrences (all)	12 / 225 (5.33%) 12		
Tenderness (Significant): After toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative assessment type: Systematic subjects affected / exposed[101] occurrences (all)	0 / 225 (0.00%) 0		
Redness (Severe): After toddler dose	Additional description: Subjects affected and occurrences for LRs and SEs is same as data collected through e- diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed[102] occurrences (all)	1 / 225 (0.44%) 1		
Psychiatric disorders Irritability subjects affected / exposed[103] occurrences (all)	1 / 234 (0.43%) 1		
Infections and infestations Bronchitis subjects affected / exposed[104] occurrences (all)	3 / 234 (1.28%) 3		
Bronchopneumonia subjects affected / exposed[105] occurrences (all)	0 / 234 (0.00%) 0		
Gastroenteritis subjects affected / exposed[106] occurrences (all)	0 / 234 (0.00%) 0		
Gingivitis			

subjects affected / exposed[107]	0 / 234 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed[108]	0 / 234 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed[109]	34 / 234 (14.53%)		
occurrences (all)	43		
Oral candidiasis			
subjects affected / exposed[110]	0 / 234 (0.00%)		
occurrences (all)	0		
Oral fungal infection			
subjects affected / exposed[111]	0 / 234 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed[112]	1 / 234 (0.43%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed[113]	0 / 234 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed[114]	1 / 234 (0.43%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed[115]	19 / 234 (8.12%)		
occurrences (all)	20		
Tracheitis			
subjects affected / exposed[116]	0 / 234 (0.00%)		
occurrences (all)	0		
Viral skin infection			
subjects affected / exposed[117]	1 / 234 (0.43%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Calcium deficiency			
subjects affected / exposed[118]	0 / 234 (0.00%)		
occurrences (all)	0		

Notes:

[18] - 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: Here number of subjects exposed signifies subjects evaluable for adverse event.

[19] - 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: Here number of subjects exposed signifies subjects evaluable for adverse event.

[20] - 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: Here number of subjects exposed signifies subjects evaluable for adverse event.

[21] - 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: Here number of subjects exposed signifies subjects evaluable for adverse event.

[22] - 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: Here number of subjects exposed signifies subjects evaluable for adverse event.

[23] - 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: Here number of subjects exposed signifies subjects evaluable for adverse event.

[24] - 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: Here number of subjects exposed signifies subjects evaluable for adverse event.

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Justification: Here number of subjects exposed signifies subjects evaluable for adverse event.

[26] - 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: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all 7 days.

[27] - 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.
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[43] - 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.
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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